

# WRAIR

Walter Reed Army  
Institute of Research

# 125

YEARS  
1893-2018



Soldier Health • World Health  
UNCLASSIFIED

# Scientists and Soldiers: the unique heritage of **WRAIR Neuroscience**

Dale C Smith, PhD

Professor of Military Medicine & History

Department of Military & Emergency Medicine

Uniformed Services University of the Health Sciences

14 November 2018



Walter Reed Army  
Institute of Research

**125**

YEARS  
1893-2018

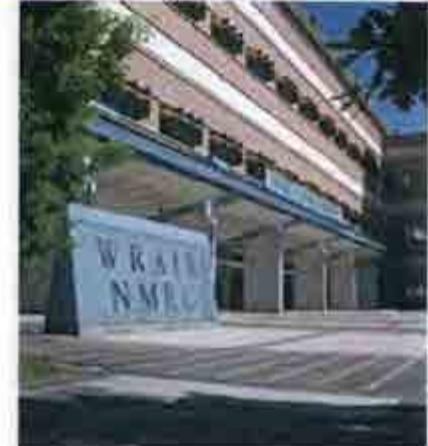




# **WRAIR @ 125ae.**

## **Army Medical R & M Command**

### **Still teaching but not primarily a school**

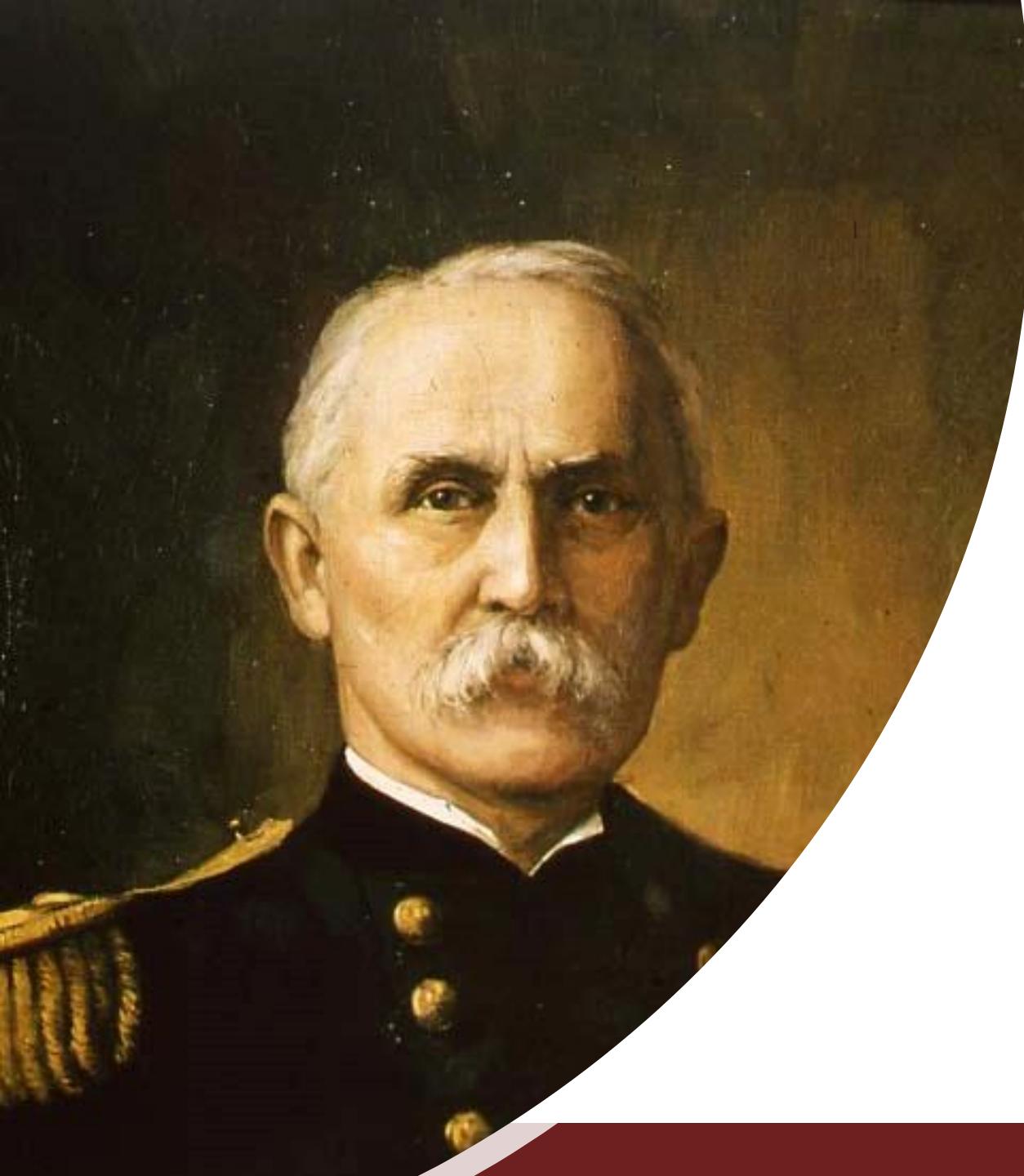


- Post Goldwater Nichols
- Post BRAC
- New Science
- New Technology
- New Threats

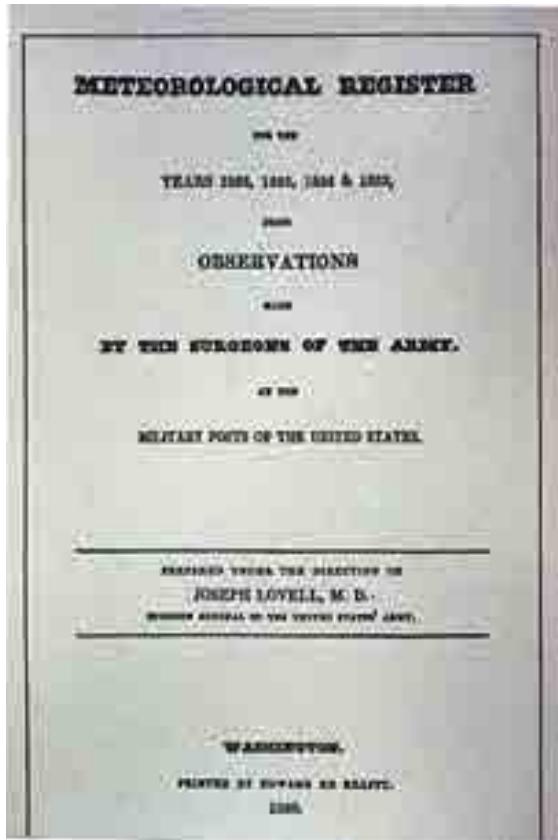
# **Benjamin Franklin**

**“Historians relate,  
not so such what is  
done, as what they  
would have  
believed.”**





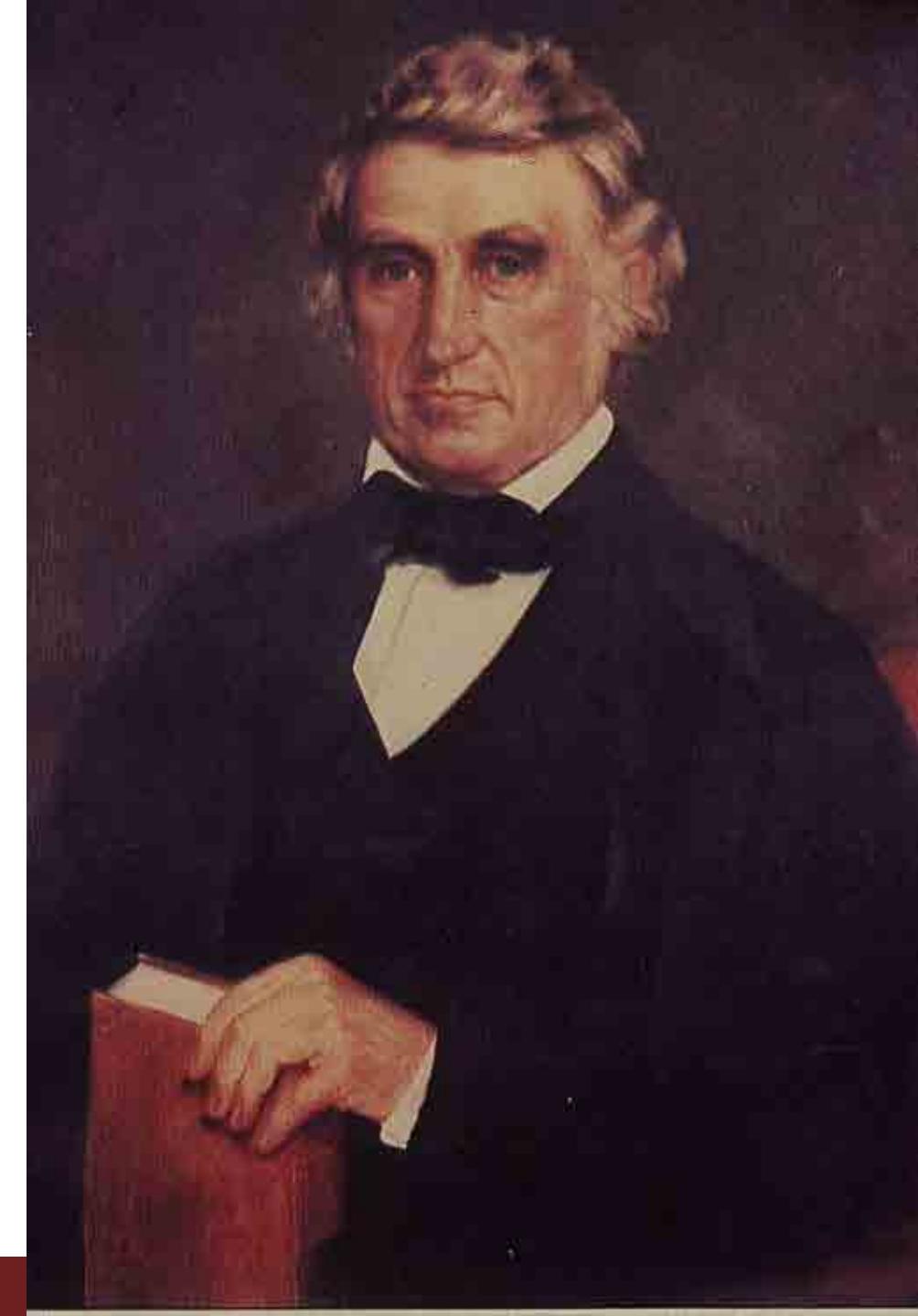
**BG  
Sternberg,  
TSG, 1893**

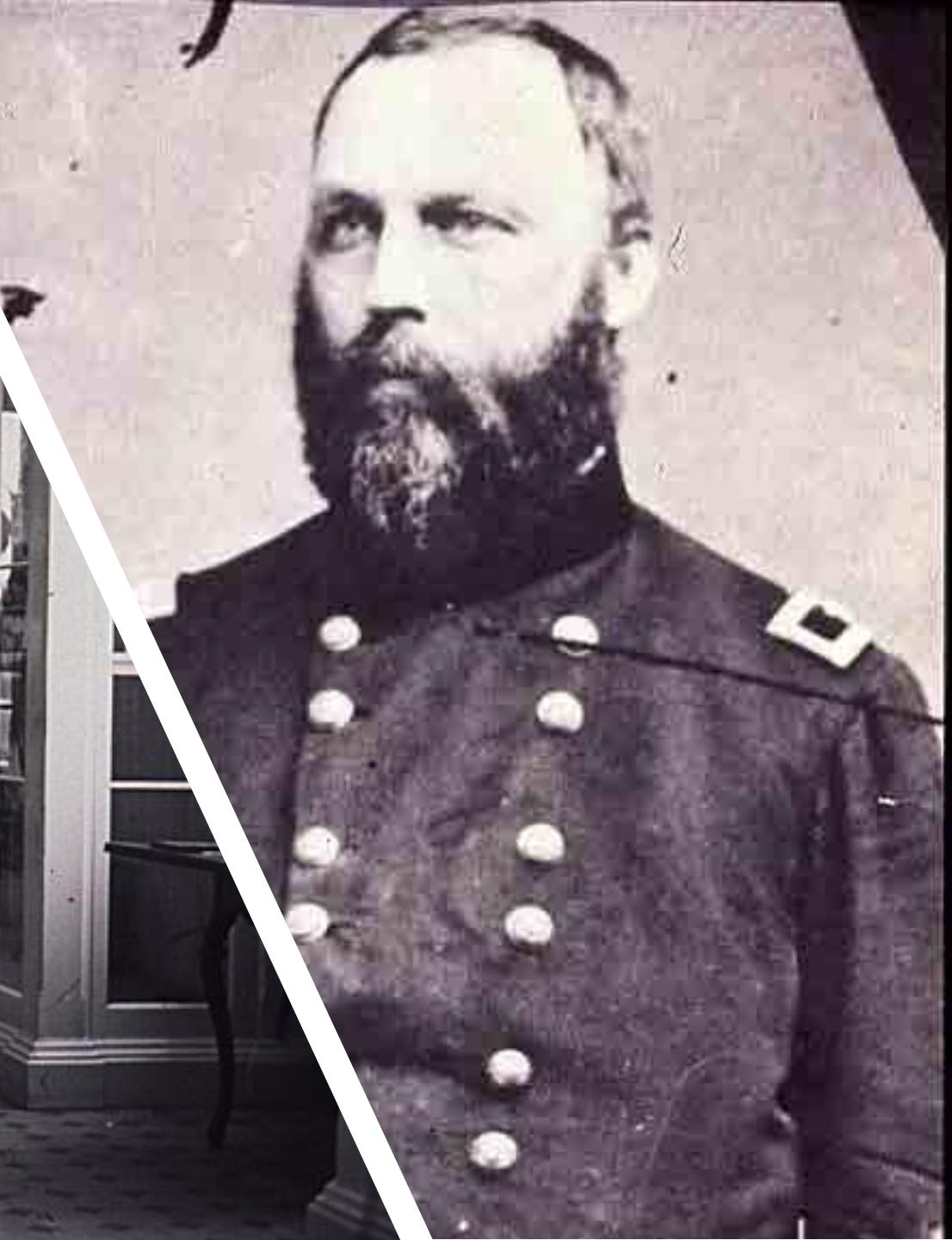


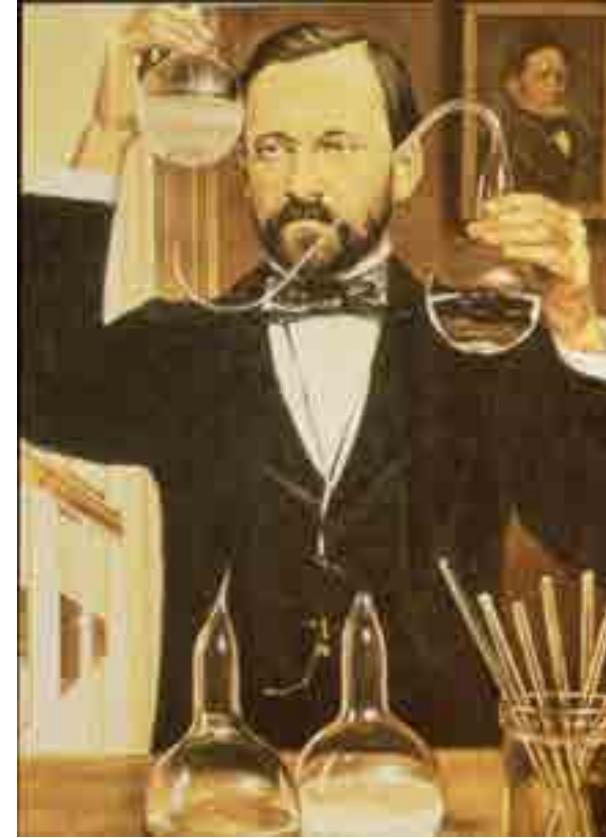
# Joseph Lovell, TSG

# **William Beaumont & Digestion**

- TSG personal support
- Consultants
- Personnel issues
- Released time



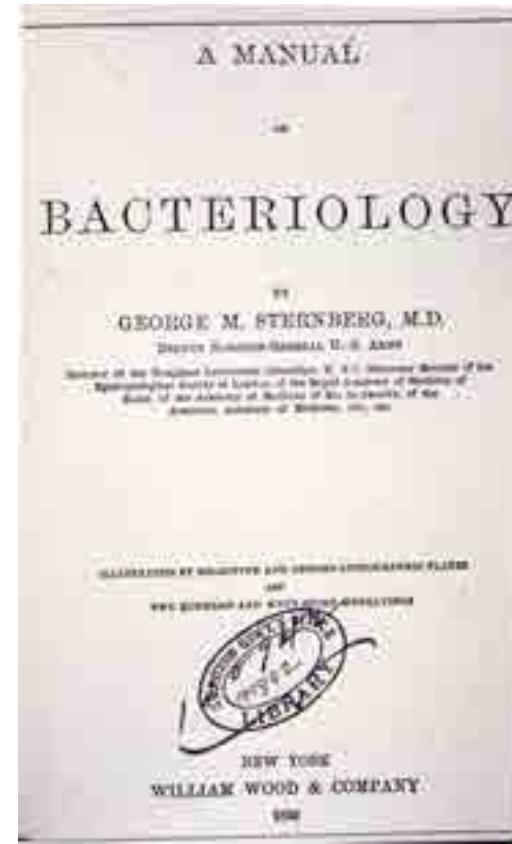




# Germ Theories & Medical Research



||

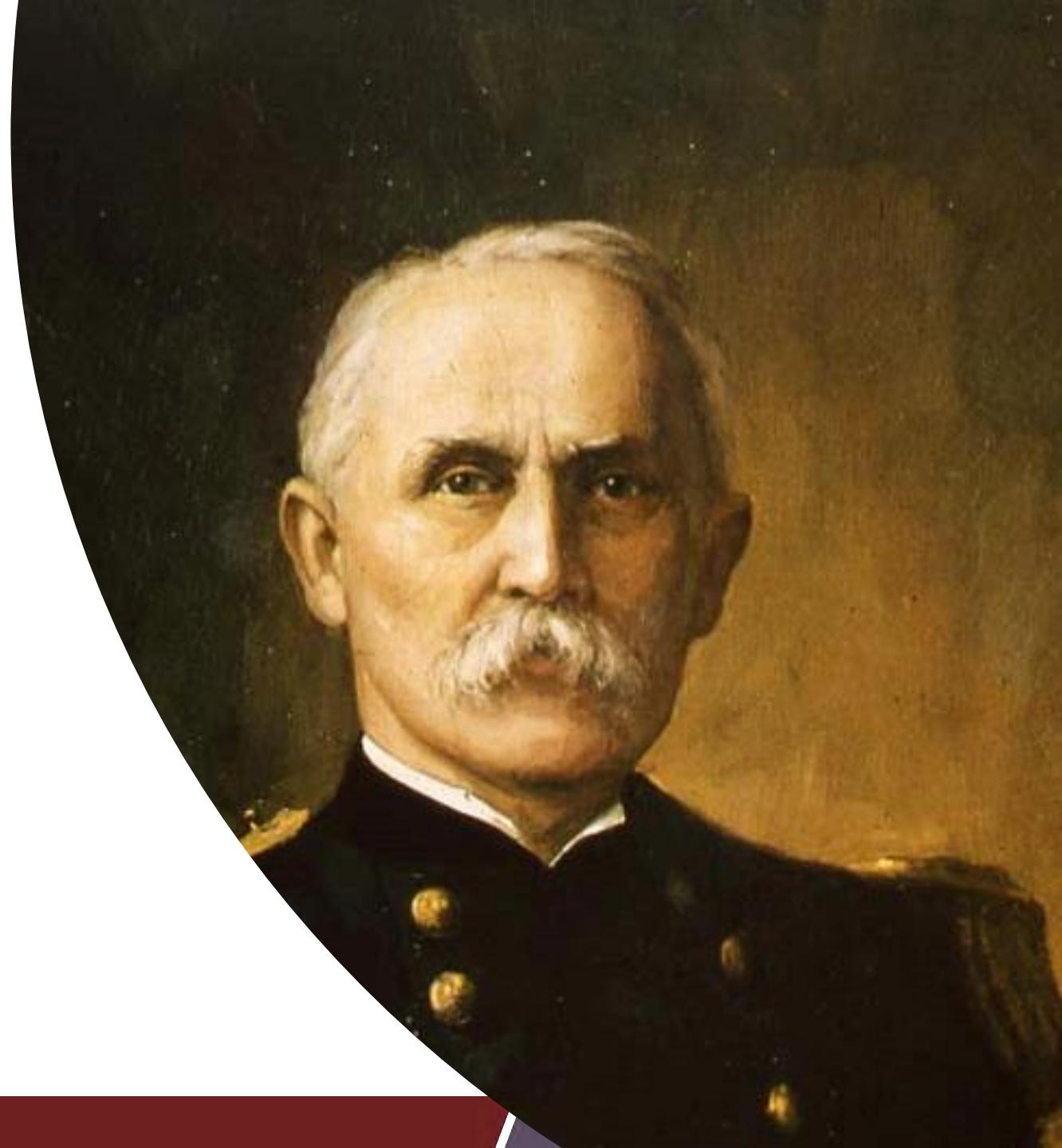


Personal research: microscopy, disinfection, and germs

---

European travel & study

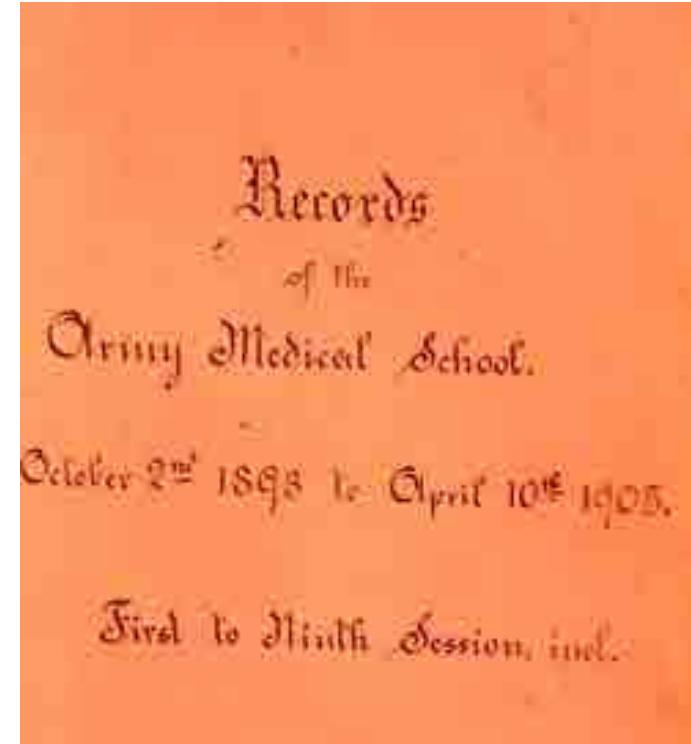
**The challenge of  
education and the  
new medicine: learn  
by doing from faculty  
doing research**





# Faculty

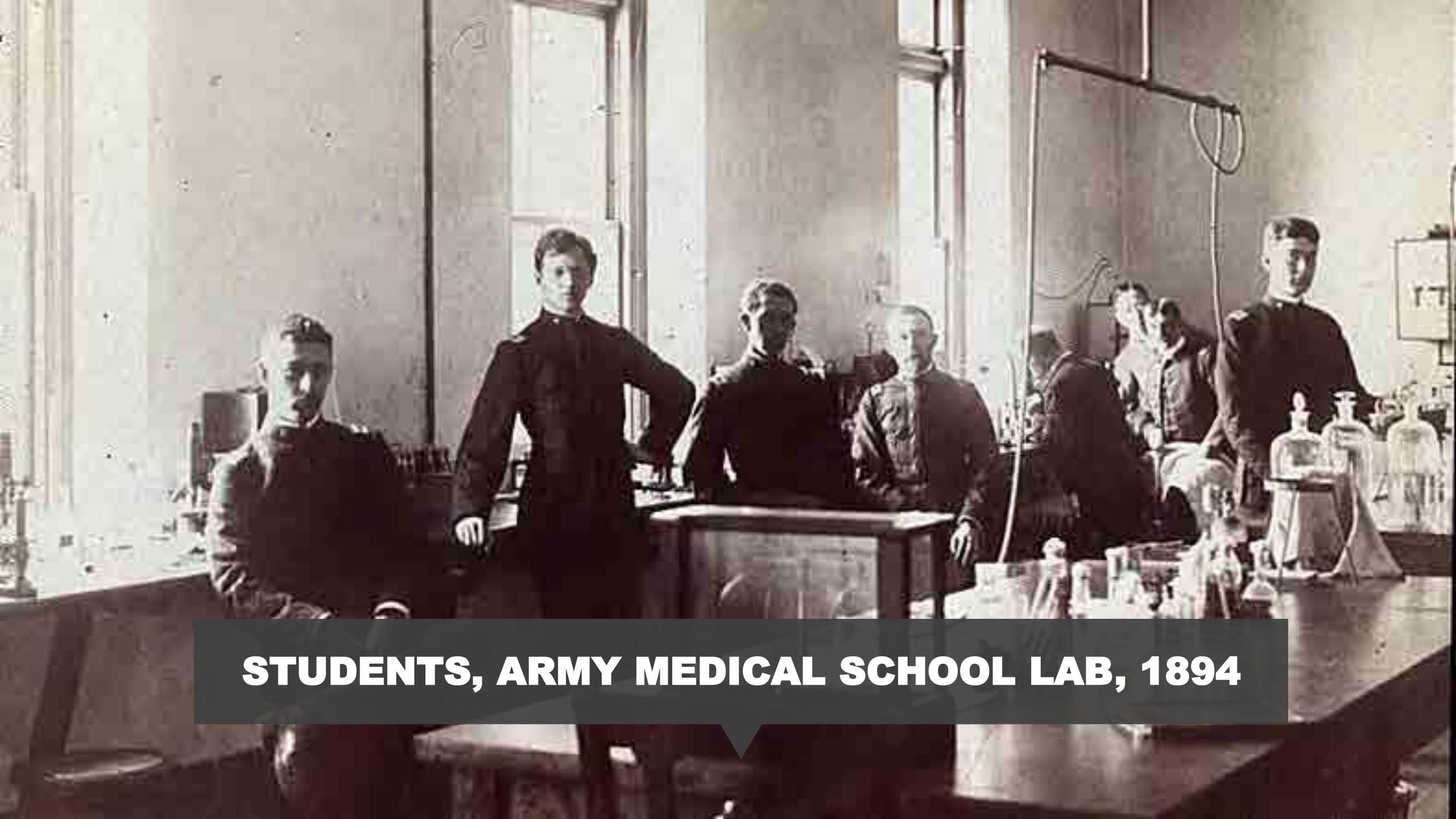
- COL Alden, President
- LTC Forwood, Military Surgery
- MAJ Smart, Military Medicine
- Dr Billings, Military Hygiene
- CPT Reed, microscopy
- CPT Cabell, HC Drill



# Walter Reed as “Dean”

[i.e. secretary of the faculty]

UNCLASSIFIED



**STUDENTS, ARMY MEDICAL SCHOOL LAB, 1894**

# Army Medical School

---

- Isolation
- Scientific opportunity
- First school to emphasize prevention

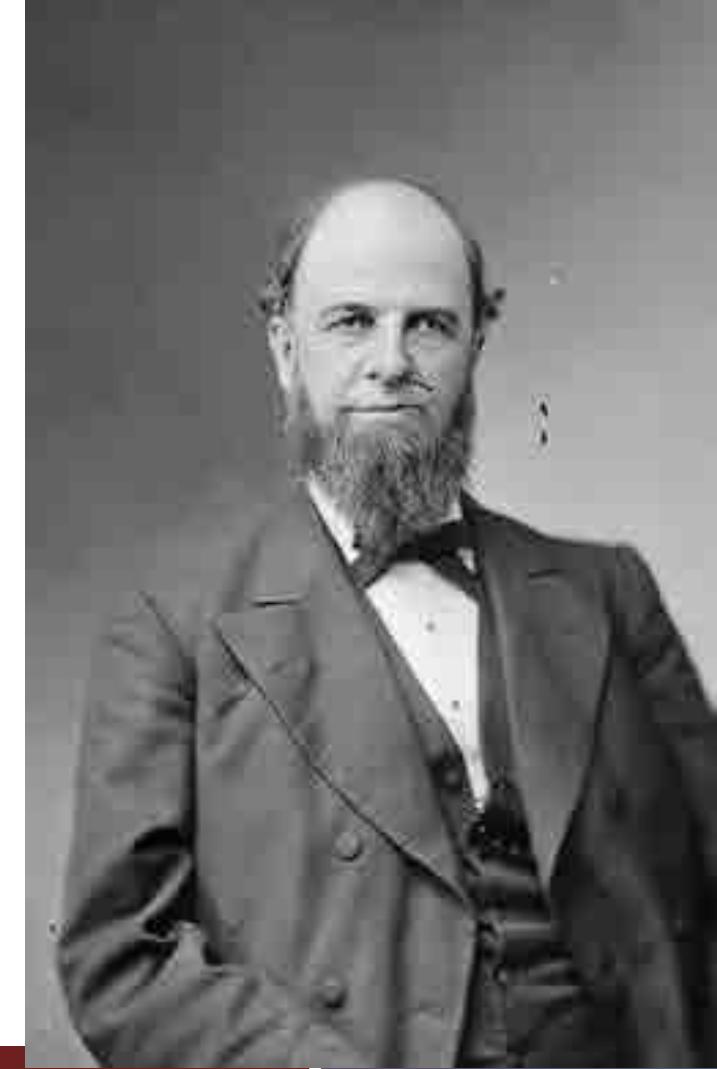


Olser

# Faculty 2<sup>nd</sup> year additions

- COL Alden, President
- LTC Forwood, Military Surgery
- MAJ Smart, Military Medicine
- Dr Billings, Military Hygiene
- CPT Reed, microscopy
- CPT Cabell, HC Drill
- Dr W.W. Godding, Psychiatry
- Dr Stiles, USPHS, tropical parasites

# [St Elizabeth's Hospital] & Dr. Godding





# War with Spain



# Army Medical Museum & School

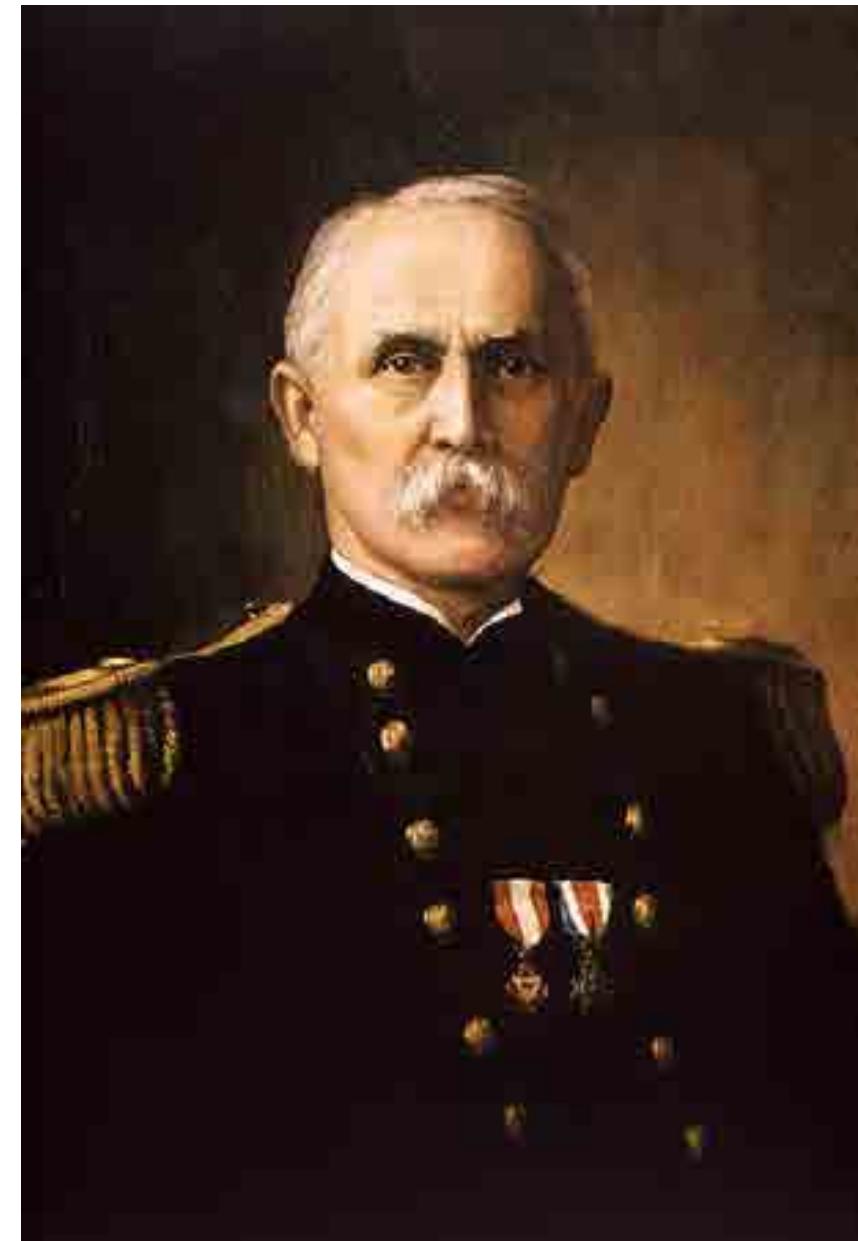
## Original Articles.

---

SANITARY LESSONS OF THE WAR.\*

BY GEORGE M. STERNBERG, M.D., L.L.D.

SURGEON-GENERAL U. S. A.



# The Great European War



A Nation promises to care for those it sends into harm's way



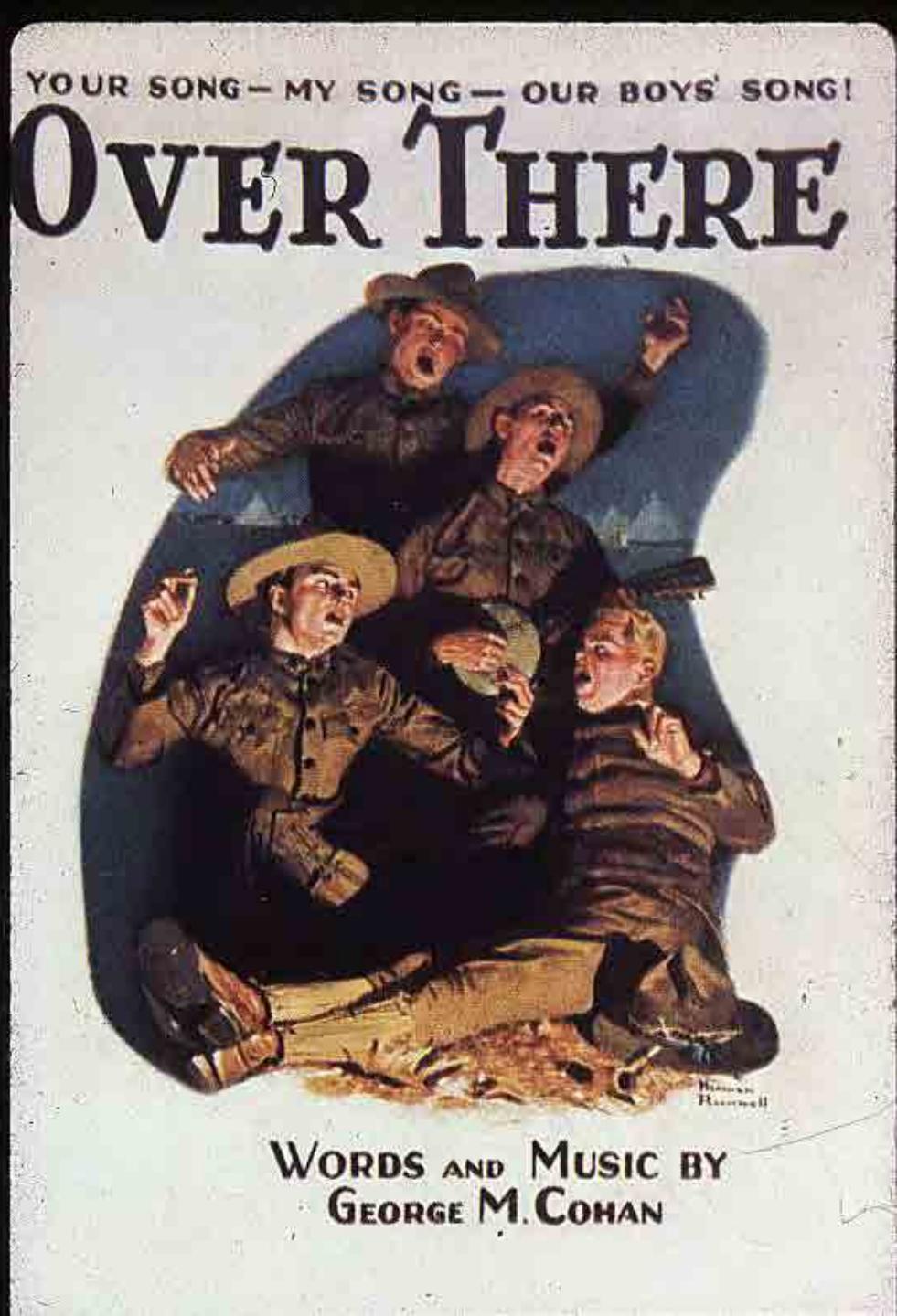




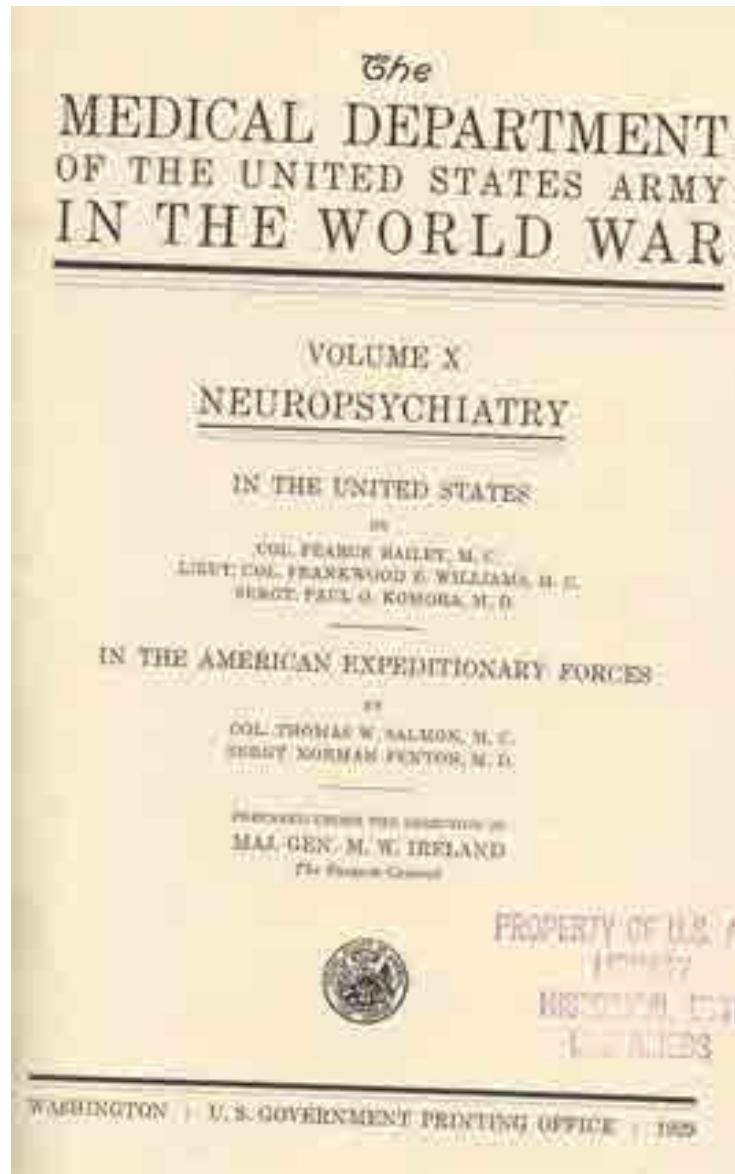
## **Charles Craig & Education of Laboratory workers**



Ireland







Washington, D. C.

**Army  
Medical  
Center  
est. 1923**



Army Medical  
Professional Service  
School

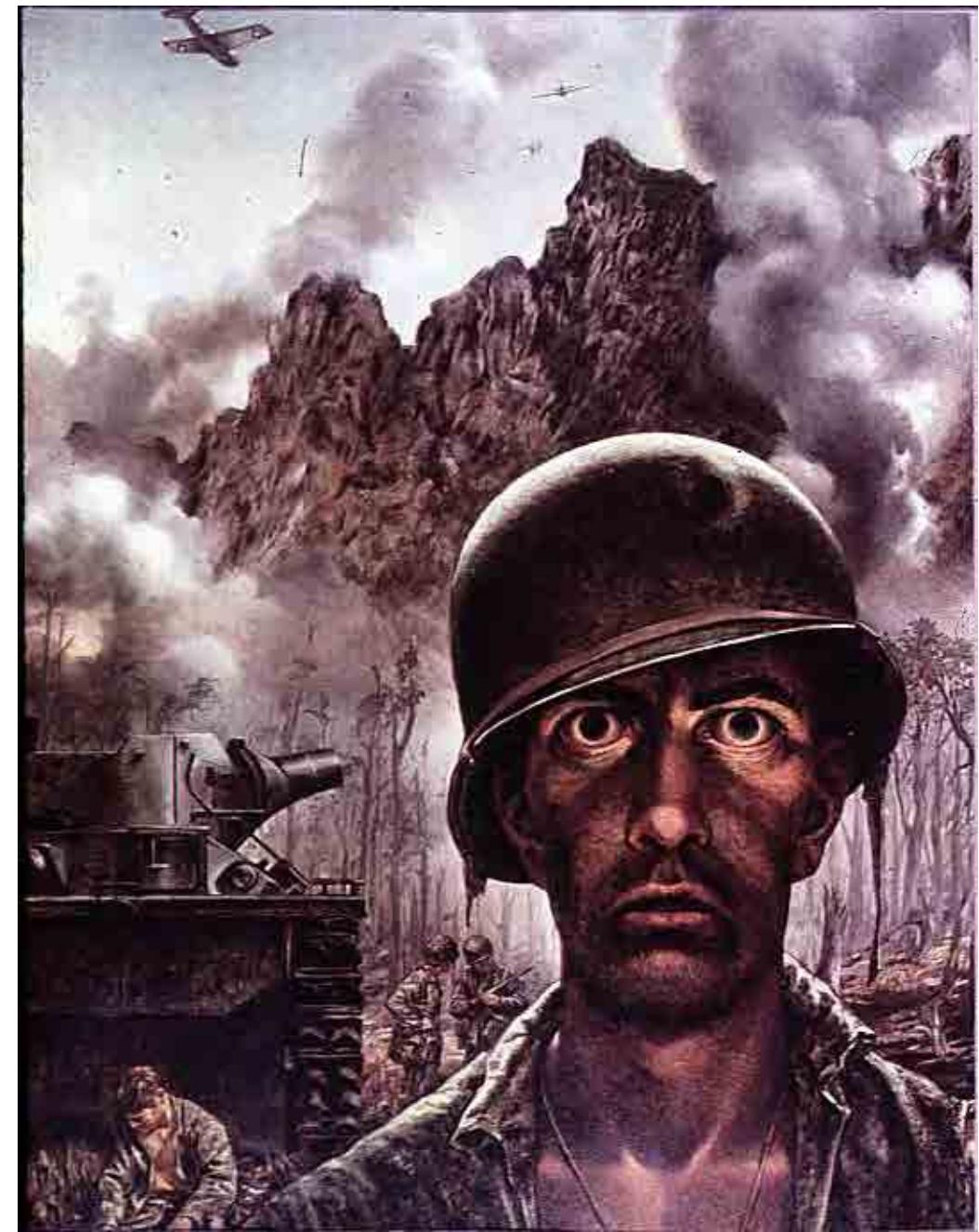
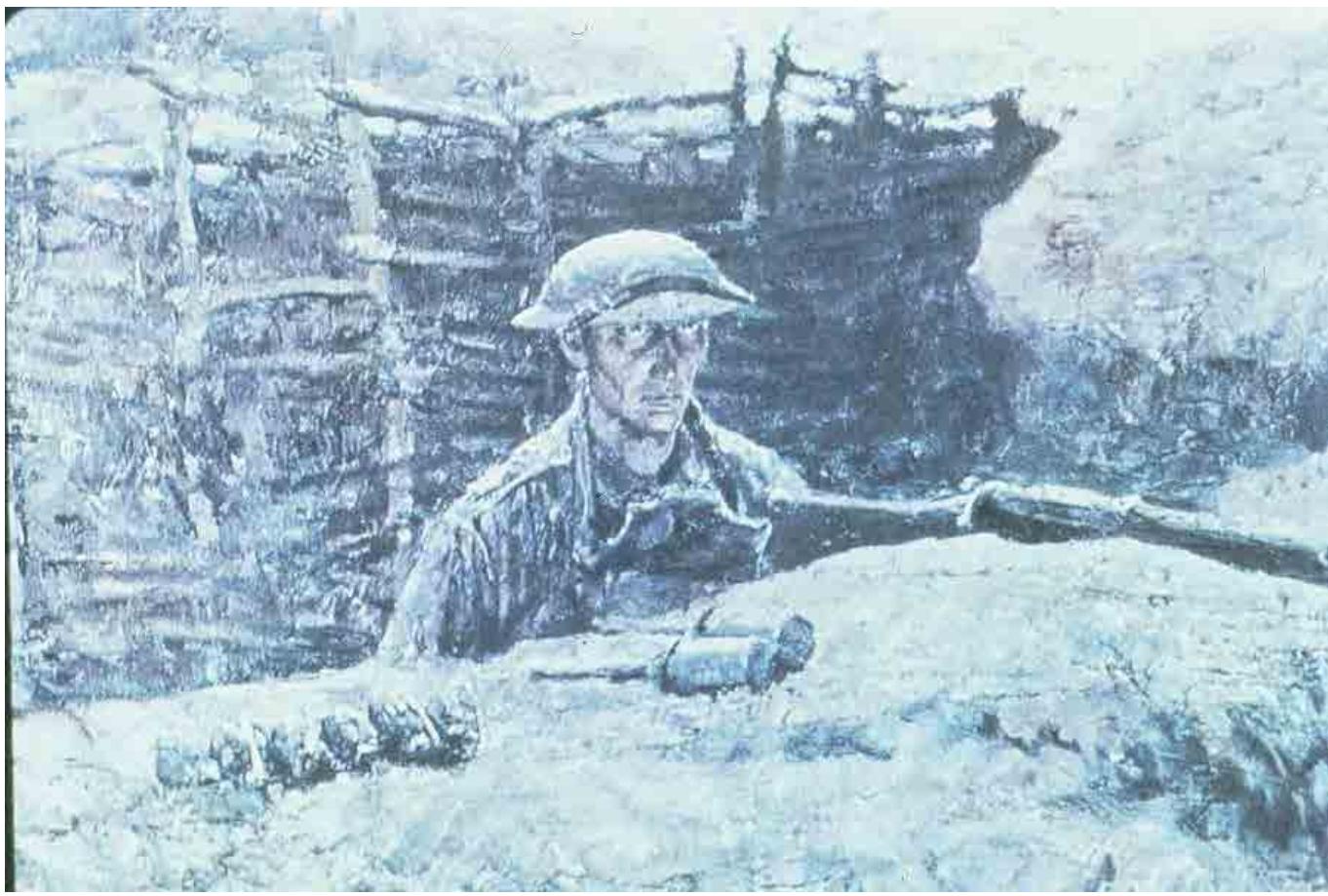
# Science

- Penicillin
- Blood products
- etc.

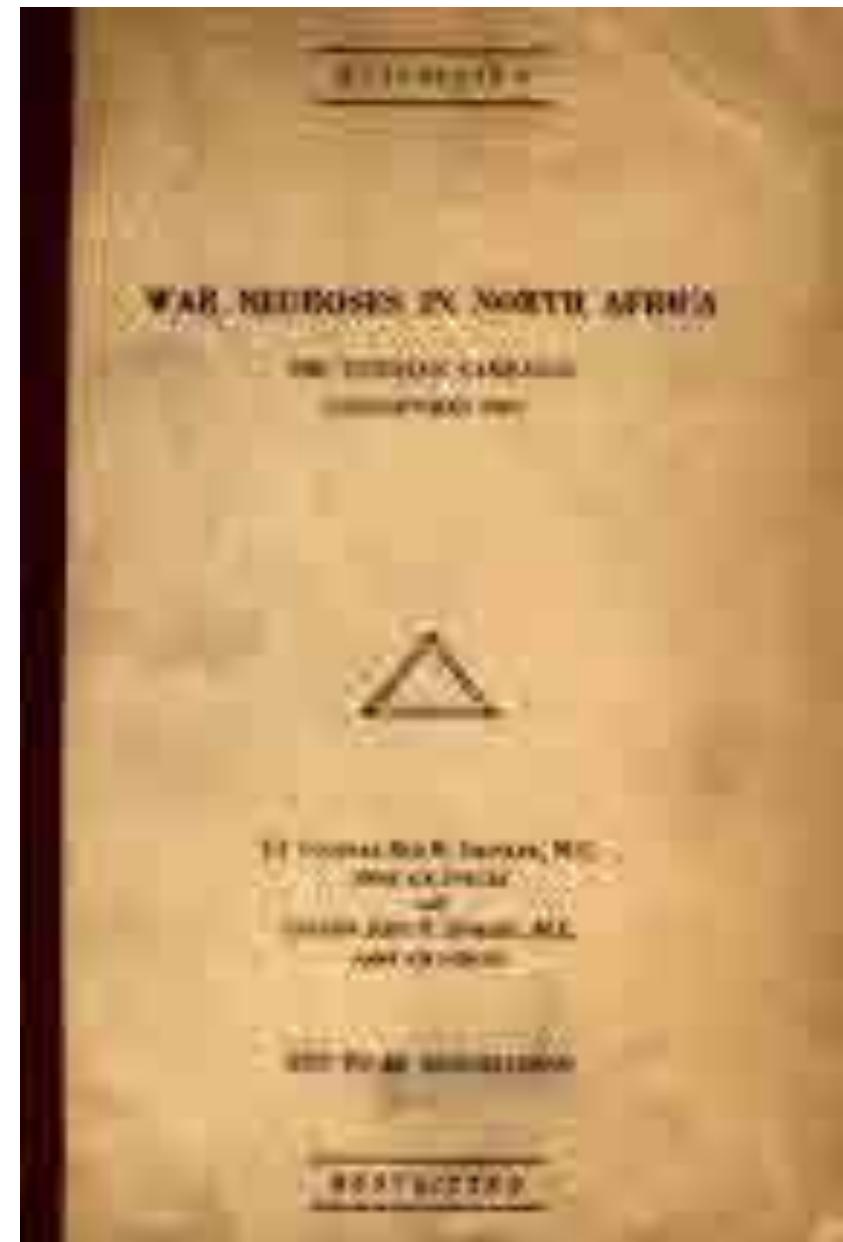
# Distribution

40% MDs, 8% pop.

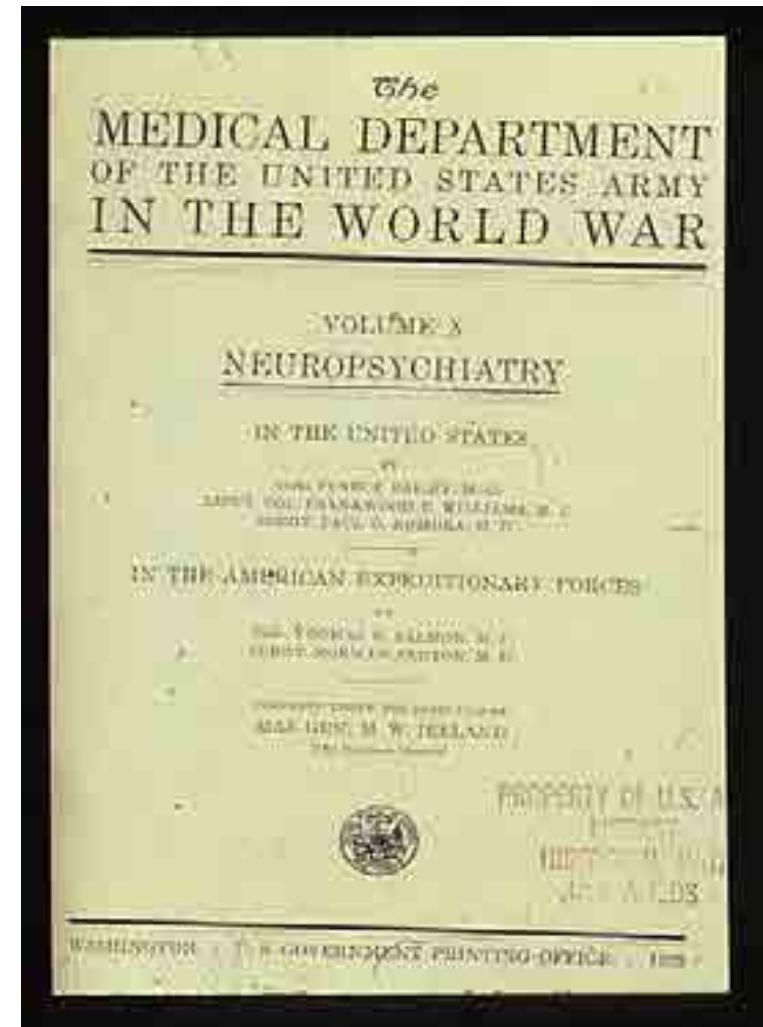




# 20% of Casualties were NP



# Lessons Learned



# **Frederick Hanson**



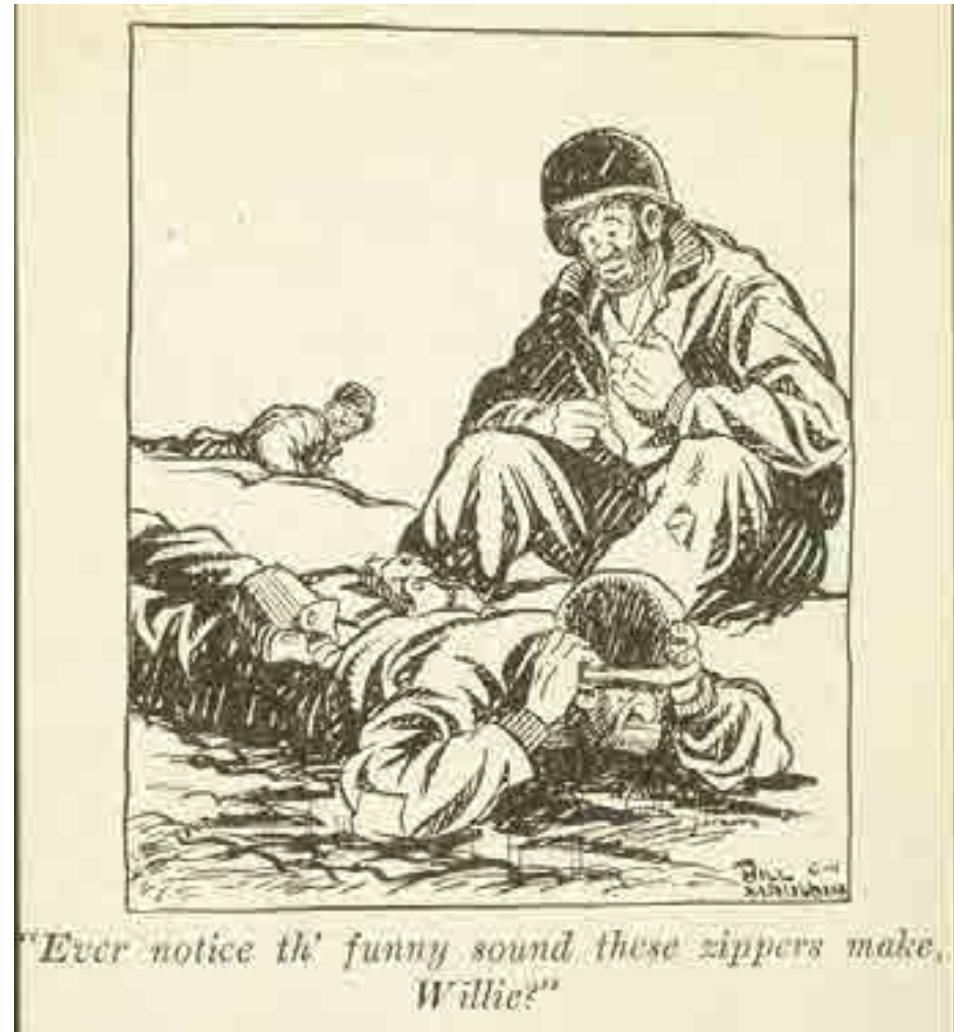
**95 patients with 63%  
RTD /p 4 days rest**

**FIFTH ARMY NEUROPSYCHIATRIC CENTER  
(250 BEDS) < 3% RTD**

**WAS A TREATMENT FACILITY  
AND  
TEACHING CENTER FOR PSYCHIATRISTS**



# Battle Fatigue



*"Ever notice th' funny sound these zippers make,  
Willie?"*



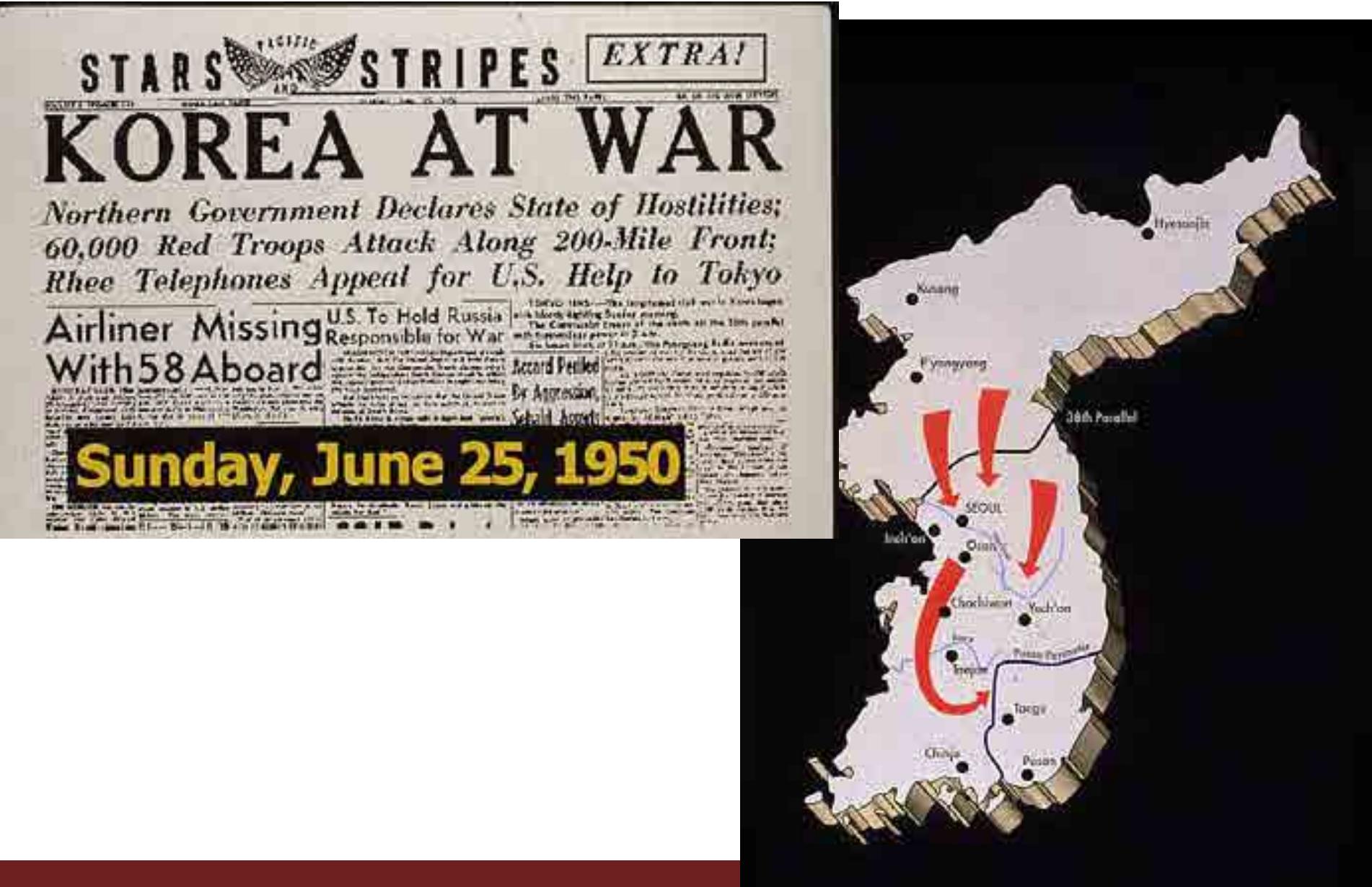
**Army Medical  
& Graduate  
School**

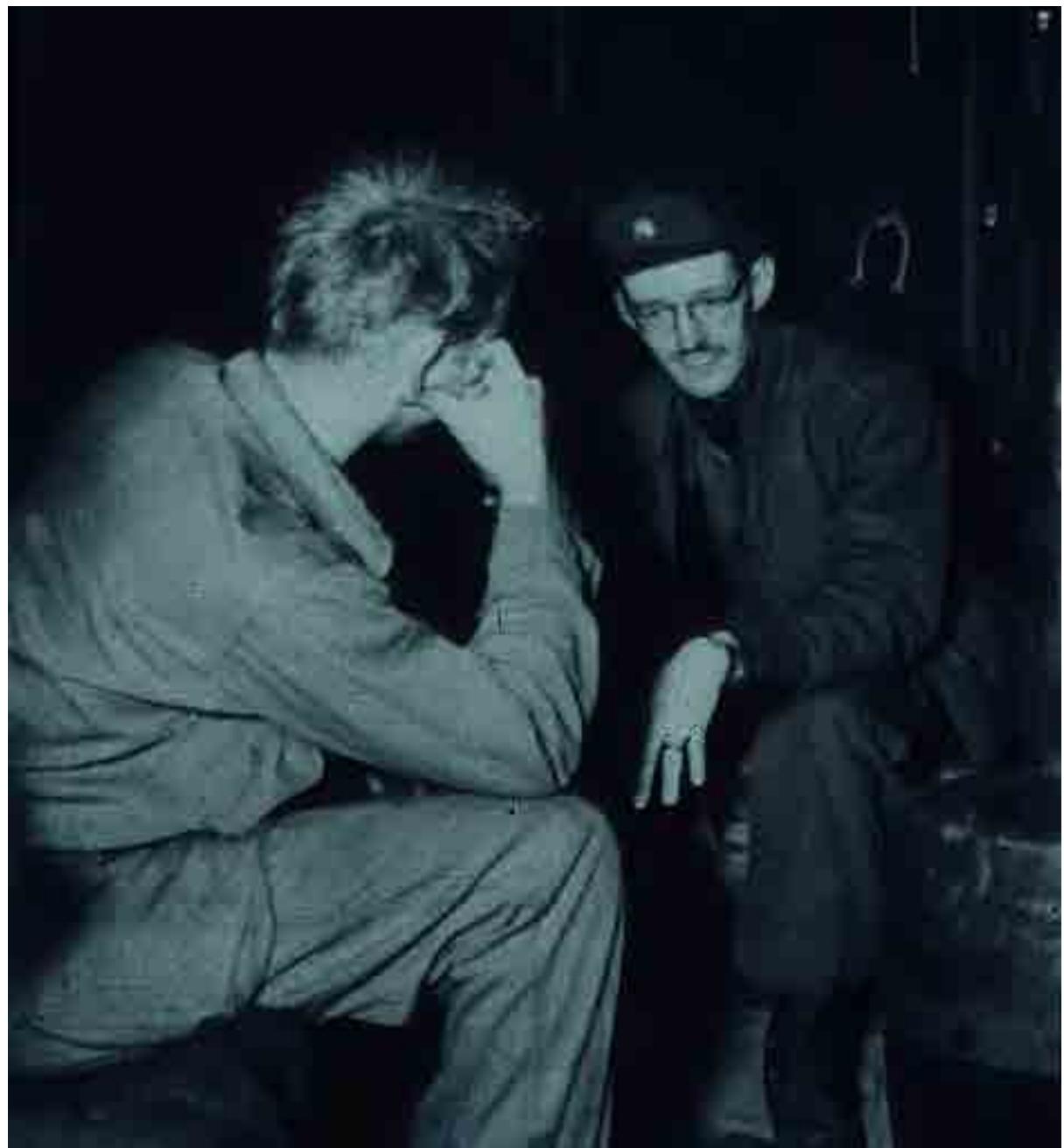
---

1947

# Military GME









Hans Selye

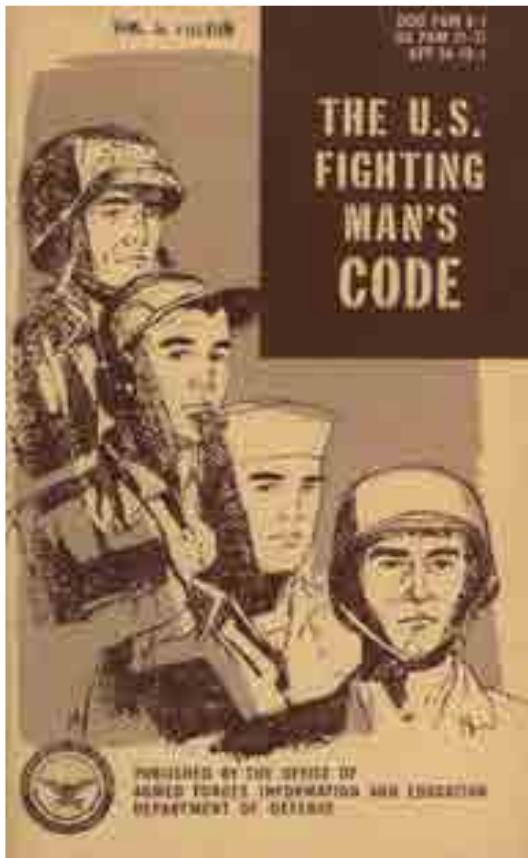
# Korean War Observations

SOME GENERAL  
CONSIDERATIONS OF  
HOMEOSTATIC AND ADAPTIVE  
MECHANISMS TO STRESS IN  
EFFECT PRIOR TO  
WOUNDING\*  
STANLEY H. ELDRED, M. D.



F Gentry Harris

# Character Debate



The image shows the title page of the "CODE OF CONDUCT". At the top, five military seals are displayed: the Department of Defense seal, the Army seal, the Navy seal, the Marine Corps seal, and the Air Force seal. Below the seals, the title "CODE OF CONDUCT" is centered. The document is organized into six numbered sections (I through VI), each containing a statement of principle.

**I** I am an American, fighting in the forces which guard my country and our way of life. I am prepared to give my life in their defense.

**II** I will never surrender of my own free will. If in command I will never surrender the members of my command while they still have the means to resist.

**III** If I am captured I will continue to resist by all means available. I will make every effort to escape and aid others to escape. I will accept neither parole nor special favors from the enemy.

**IV** If I become a prisoner of war, I will keep faith with my fellow prisoners. I will give no information or take part in any action which might be harmful to my comrades. If I am senior, I will take command. If not, I will obey the lawful orders of those appointed over me and will back them up in every way.

**V** When questioned, should I become a prisoner of war, I am required to give name, rank, service number, and date of birth. I will evade answering further questions to the utmost of my ability. I will make no oral or written statements disloyal to my country and its allies or harmful to their cause.

**VI** I will never forget that I am an American, fighting for freedom, responsible for my actions, and dedicated to the principles which made my country free. I will trust in my God and in the United States of America.



## **Walter Reed Army Institute of Research (1953)**

---

---

# **Barry Plan**

Research &  
GME role



# Neuropsychiatry



David H.  
Hubel



Robert  
Galambos



David Rioch



Edward R. Perl



WALLE J. H. NAUTA

# Issues of Neuro psychiatry

- Combat reaction
- Nuclear war & panic
- Stress, sleep deprivation, world movement issues

## **Issues of Neuro psychiatry**

- Combat reaction
  - World War II
  - Korean Lessons
  - Lessons not learned

# **Issues of Neuro psychiatry**

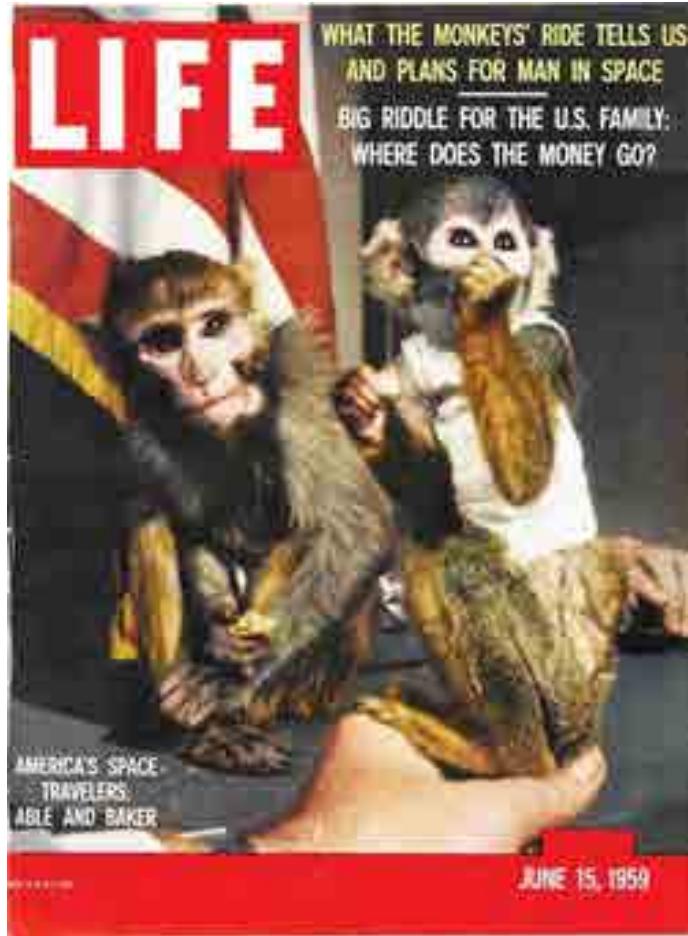


- Combat reaction
- Nuclear war & panic
  - Lack of Social Sciences
  - Lack of clear mission
- Stress, sleep deprivation, world movement issues



## **James S. Ketchum Incapacitating weapons clinical program**

# Joseph V Brady, MSC



# Leonard Heaton, TSG



- Grow GME
- Expand professional pay
- Create separate promotion pathway
- Remove MC officers from non clinical roles

# Physiology to Psychology

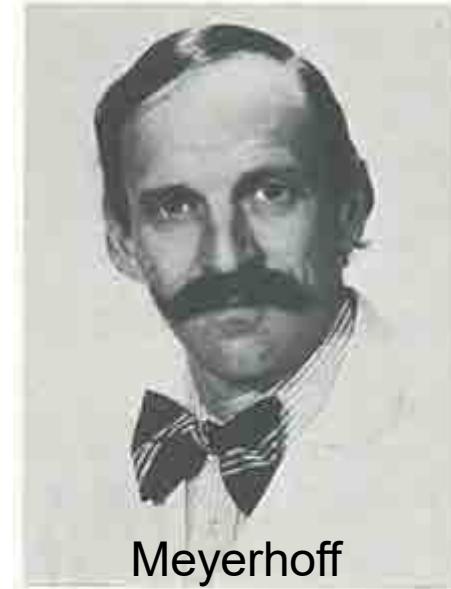


## Stress

Psychology  
to  
Physiology



- Brady, J. V. 1958. Ulcers in "executive" monkeys. *Scientific American*, 199(3): 95-104.



Meyerhoff



Mougey

# Vietnam



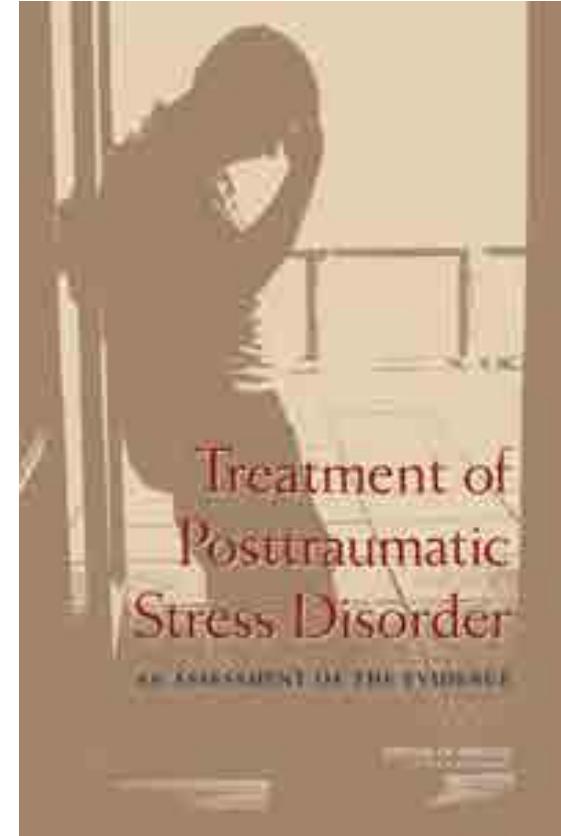
# Casualties Vietnam

Cause	Rate (Admissions per Thousand)					
	1965	1966	1967	1968	1969	1970
Wounded	61.6	74.8	84.1	120.4	87.6	52.9
NP casualty	11.7	12.3	10.5	13.3	15.8	28.1
Viral Hepatitis	5.7	4.0	7.0	8.6	6.4	7.2
STD /c CRO	277.4	281.5	240.5	195.8	199.5	222.9
STD /s CRO	3.6	3.8	2.6	2.2	1.0	1.4

F. Jones, Psychiatric Lessons of War, page 17 in *War Psychiatry* (Washington, Borden Institute, 1995)

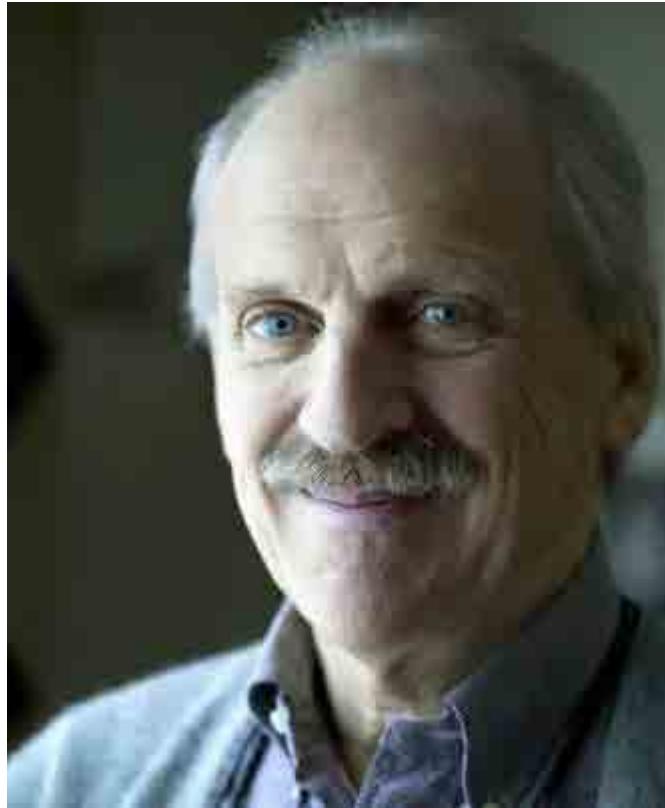
# Individual Replacement





# Medical Science & Practice

# **Dr. James Meyerhoff & Neuro- Chemistry**





©RichardBlair.com



THE REPORT OF  
**THE PRESIDENT'S COMMISSION  
ON AN ALL-VOLUNTEER  
ARMED FORCE**



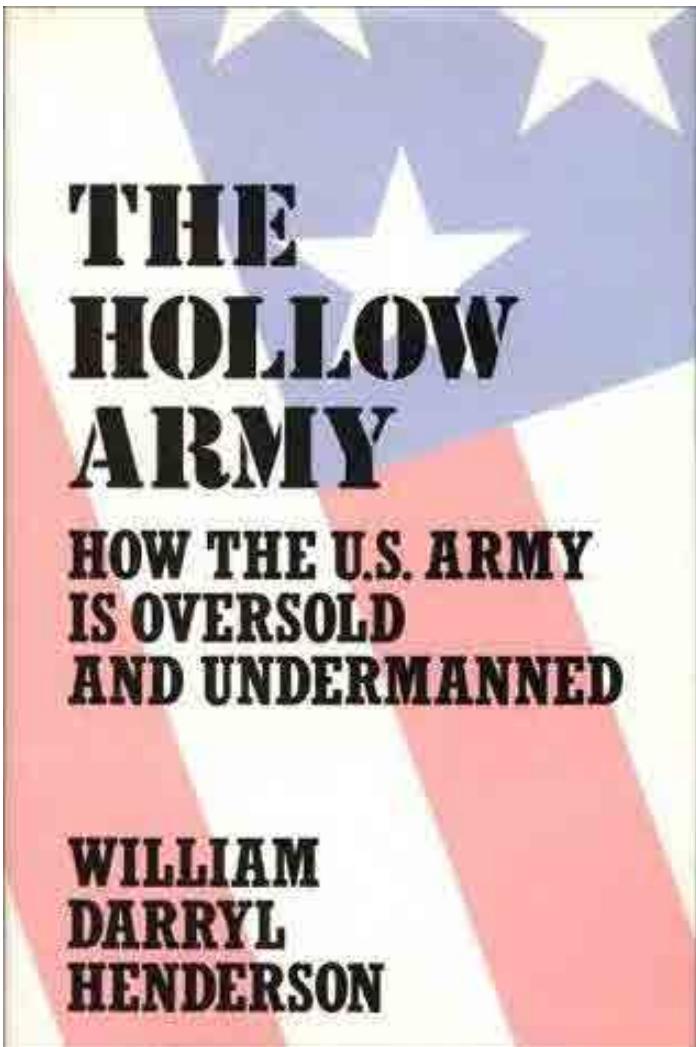
# “Hollow Army”

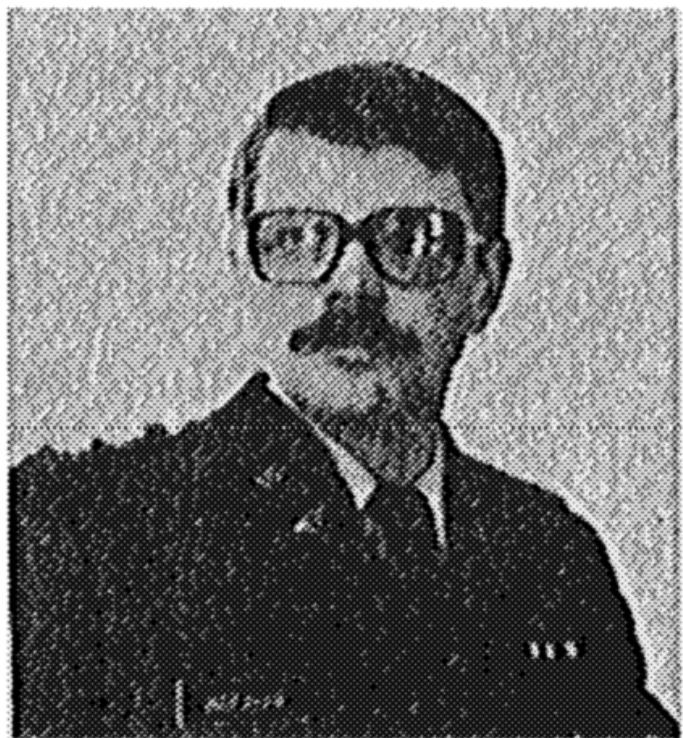


Chief of Staff US Army  
Edward C Meyer

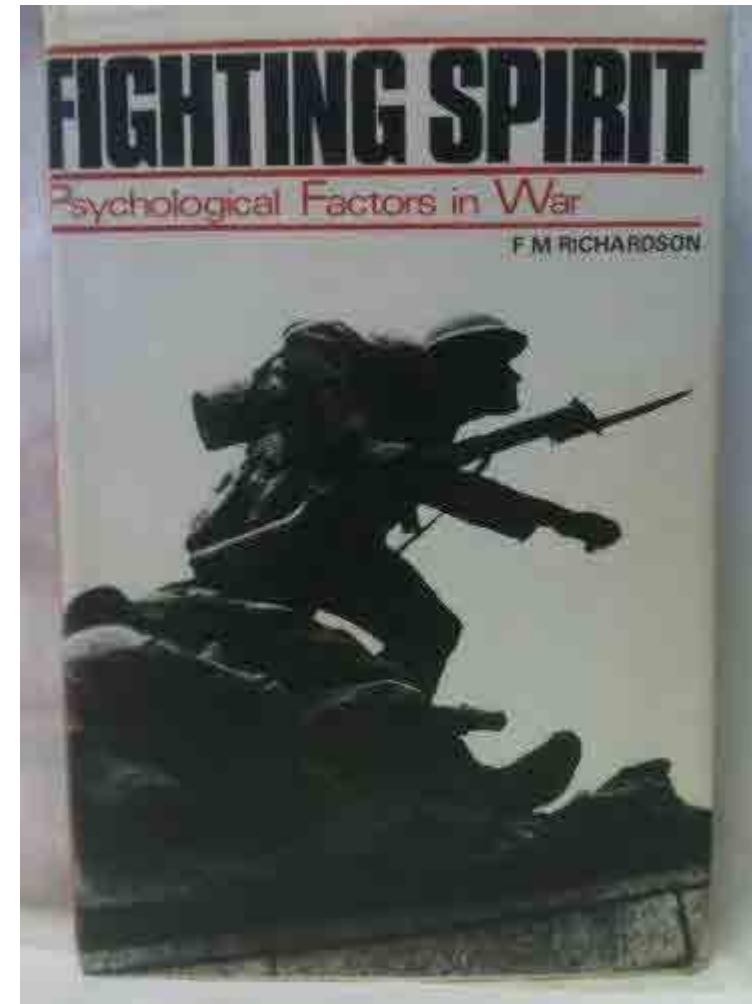


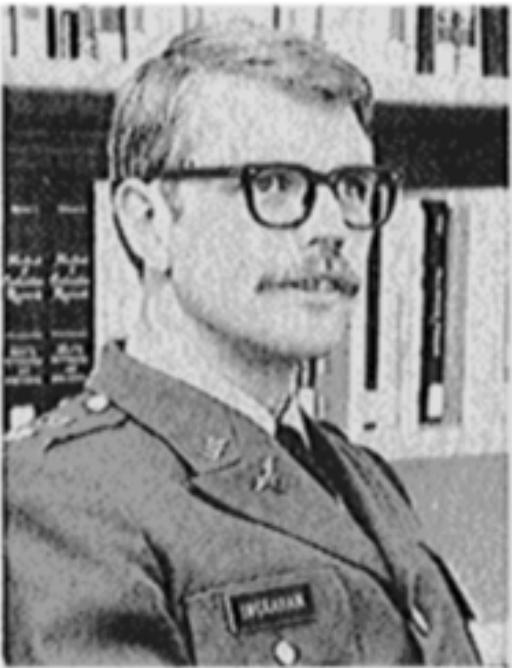
Post Vietnam conversion to All  
volunteer force -- socio economic  
issues impacted recruiting and  
readiness



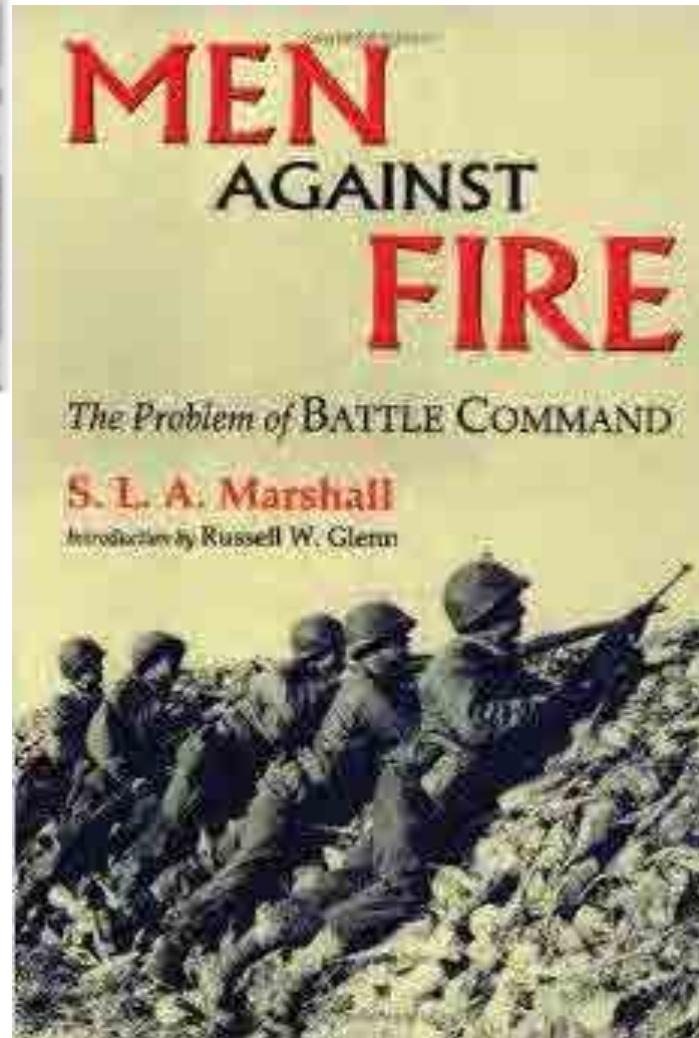


Lawrence H Ingraham, MSC



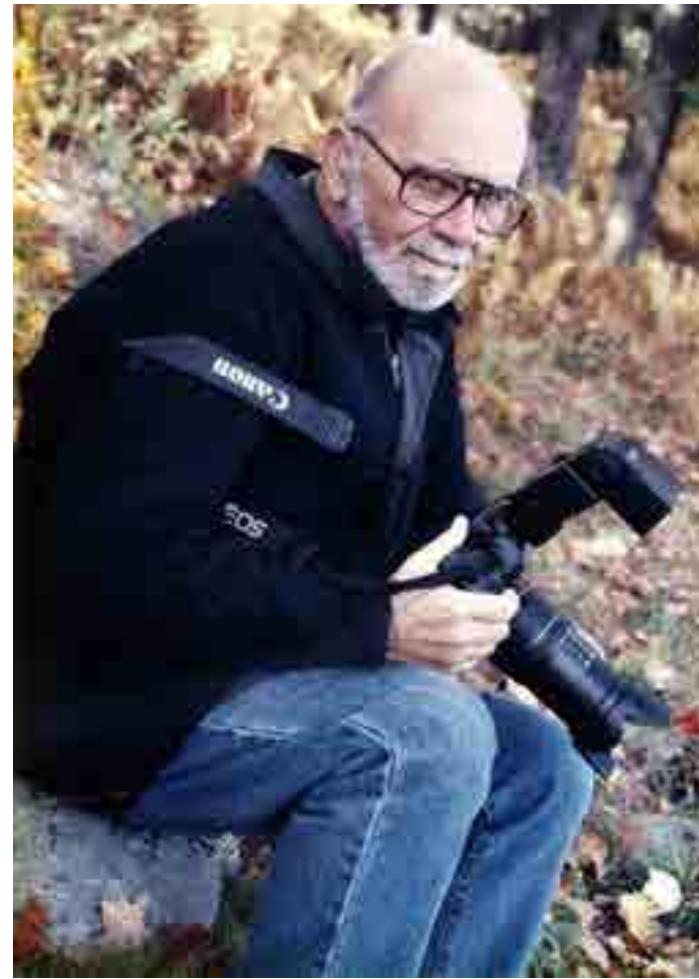
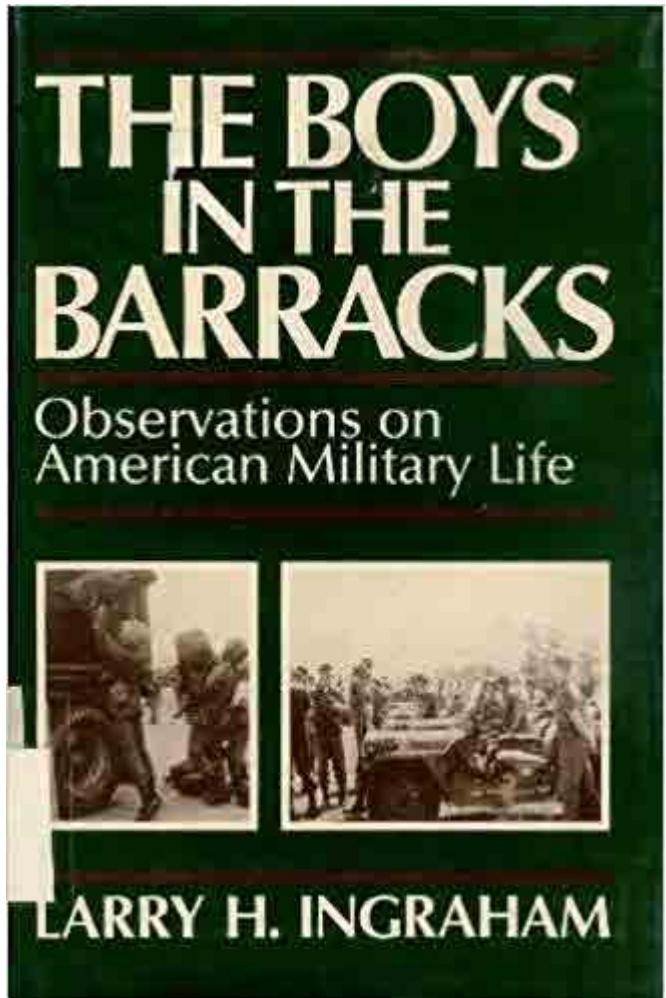


# Profession of Arms



## Leadership & Training





David H Marlowe, PhD

## UNIT MANNING SYSTEM FIELD EVALUATION

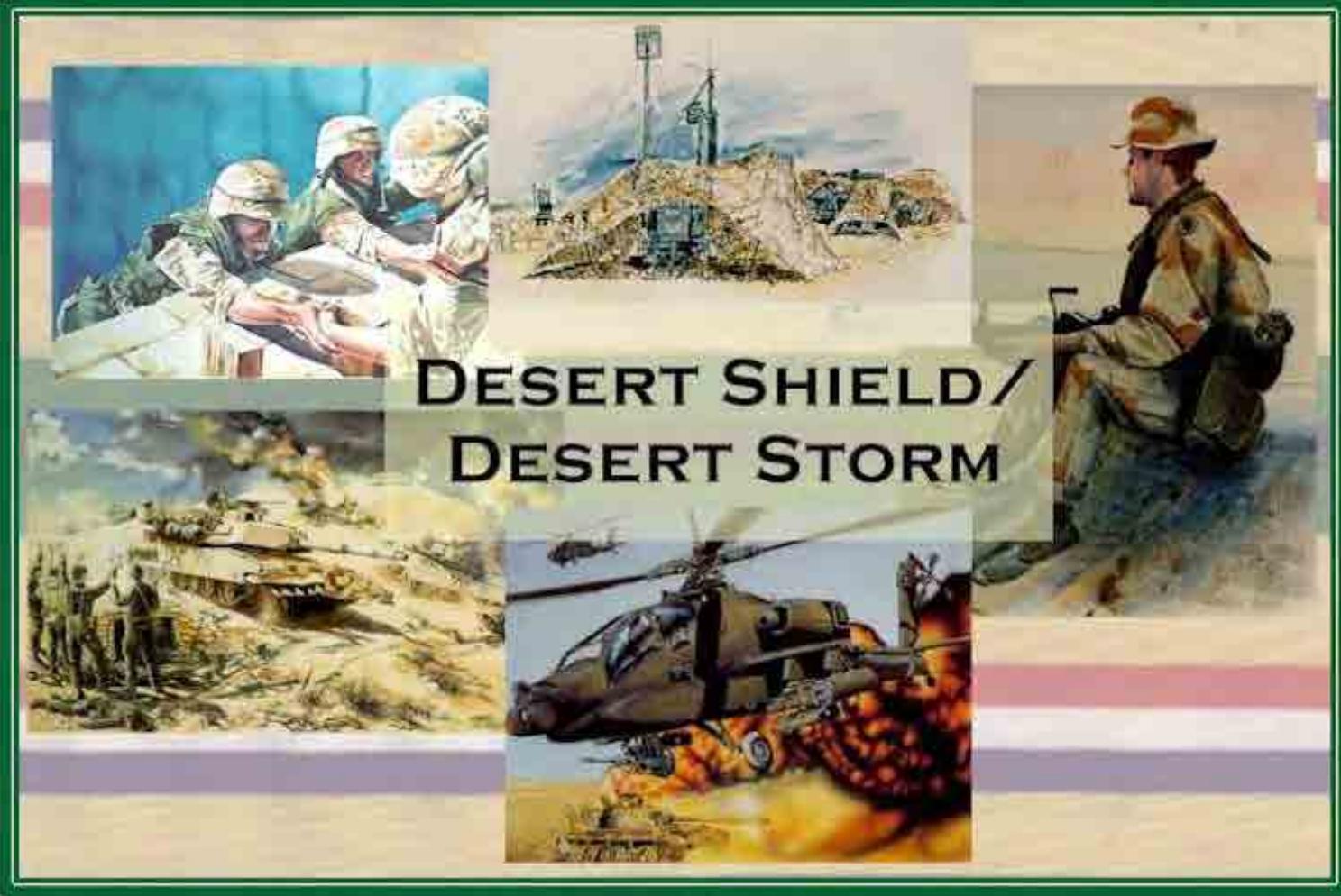
Technical Report No. 5

David H. Marlowe, Ph.D., Chief  
Department of Military Psychiatry  
Walter Reed Army Institute of Research  
Washington, D.C. 20307-5100

### PRINCIPAL AUTHORS

Faris R. Kirkland, Ph.D.  
LTC Theodore P. Furukawa, Ph.D.  
Joel M. Teitelbaum, Ph.D.  
LTC Larry H. Ingraham, Ph.D.  
LTC Bruce T. Caine, Ph.D.





## DESERT SHIELD / DESERT STORM



# Soldier Health is World Heath

# 21<sup>st</sup> Century World



# WRAIR

Walter Reed Army  
Institute of Research

# 125

YEARS  
1893-2018



Soldier Health • World Health  
UNCLASSIFIED

# TBI Research in the Military: A Personal Historical Perspective

Dallas C. Hack, MD, MPH

COL, US Army (Retired)

Former Director, Combat Casualty Care Research Program

November 14, 2018

Acknowledgements:

Jason Guthrie and Michael Doidge  
Former DCOE Historians

Kenneth Curley, MD

**WRAIR**

Walter Reed Army  
Institute of Research

**125**

YEARS  
1893-2018



# Disclosures

## **Brain Health Consultant**

- American Defense International
- Center for Brain Health
- Cohen Veterans Bioscience
- CVR Medical
- Fortuna Fix
- LiteCure
- National Collegiate Athletic Association
- Pruvit
- VirTech Bio

# Lessons Forgotten and Re-Learned

## EXPERIMENTAL ALTERATION OF BRAIN BULK

LEWIS H. WEED, *Capt., Med. Corps*

AND

PAUL S. MCKIBBEN, *1st Lt., San. Corps*

*From The Army Neuro-Surgical Laboratory, Johns Hopkins Medical School,  
Baltimore, Maryland*

Received for publication March 22, 1919

In the early stages of an investigation of the factors underlying the swelling (edema) of the brain in acute infections or injuries, attention was directed to the possible relationship between the volume of the brain and the alteration in the pressure of the cerebro-spinal fluid, following intravenous injections of solutions of various concentrations (1). For in the study of cerebral edema, but little progress has in the past been made on account of the difficulty of experimental approach. This condition remains today one of the great problems in pathology of the central nervous system.

The marked changes in the pressure of the cerebro-spinal fluid, reported in the foregoing paper, were quickly found to have a definite relation to the resultant volume of the brain. Thus, following intravenous injections of strongly hypertonic solutions which markedly lowered the pressure of the cerebro-spinal fluid, definite shrinking of the brain occurred. And conversely the brain bulk was appreciably increased by the intravenous injection of hypotonic solutions, which raised the pressure of the cerebro-spinal fluid. Such changes in the size of the brain are rapidly and uniformly brought about, giving definite information as to one phase of the physiological regulation of the volume of this organ.

# More Lessons Learned & Re-Learned



Table 4. Circumstances of Injury

	No.	# Headache	# Vertigo	# Nervousness	# Irritability	# Poor Concentration	# Loss of Memory	# Fatigability	# Difficulty Sleeping
Injured, Total	864	63.1	42.7	48.1	40.6	32.4	34.5	29.7	26.4
During military operations	775	64.0	43.9	48.9	40.8	33.9	34.5	30.2	27.1
Noncombat	84	52.9	32.1	41.7	38.1	20.2	35.7	25.0	19.0
Unknown	5	80.0	40.0	40.0	60.0	--	20.0	40.0	40.0
Controls, Total	121	18.2	9.9	20.7	19.8	8.3	5.8	6.6	10.7

Although the differences were not usually large, those men who were injured in combat complained of symptoms more frequently than did those

# Civil War



John Chisholm in 1893. U.S. National Library of Medicine photo

## 1861-64

Right: Statistics on wounds and fatalities from *The Medical Surgical History of the War of the Rebellion*. Archives.org photo

Severe TBI is considered fatal in most cases before the 20<sup>th</sup> Century. The risk of infection discourages surgeons from aggressive surgery, with surgical mortality rates around 70 percent.

Standard surgical practices are recorded in the military field books for surgeons of both the Union and Confederate Armies and described in *The Medical Surgical History of the War of the Rebellion*, which appeared in three volumes between 1868-1875. The *History* divides head injuries into three main categories: “incised and punctured wounds,” “miscellaneous injuries” and “gunshot wounds.” 94 percent of all wounds were due to gunshots during the Civil War.

Confederate surgeon John Chisholm's ***Manual on Military Surgery*** is the principal surgical textbook used by Confederate Army surgeons. Perhaps best known for his invention of the Chisholm inhaler—a device for administering chloroform anesthesia—Chisholm described the characteristics of one of the most common types of severe TBI, **diffuse axonal injury (DAI)**.

Table indicating Percentage of Fatality and Relative Frequency of Shot Wounds recorded during the War of the Rebellion.

SEAT OF INJURY.	Total Cases	Fatalities			Per cent Fatal. 2.7 %	Relative Frequency.
		Recovered.	Deceased.	Undetermined Results.		
Shot Injuries of the Head.	12,089	4,273	5,476	2,340	36.9	14.91
Shot Injuries of the Face.	9,416	3,404	460	1,348	3.9	10.77
Shot Injuries of the Neck.	4,965	2,496	616	783	15.0	1.98
Shot Injuries of the Spine.	647	279	349	14	55.3	0.36
Shot Injuries of the Chest.	39,154	13,901	5,373	970	37.6	8.34
Shot Injuries of the Abdomen.	8,426	3,435	1,293	1,690	48.7	18.37
Shot Injuries of the Pelvis.	3,128	2,194	926	30	59.7	1.28
Shot Flash Wounds of the Back.	12,581	10,882	800	799	6.7	8.18
Shot Injuries of the Upper Extremities.	67,752	30,080	5,658	2,055	6.3	33.71
Shot Injuries of the Lower Extremities.	56,413	73,655	11,813	833	13.8	35.13
Aggregate.	345,750	90,340	31,389	11,904	13.6	00.00



A page from *The Medical Surgical History of the War of the Rebellion*. Archives.org photo

1864

There are over 300,000 deserters from the Union Army alone. **Many men dealt with as disciplinary problems exhibit symptoms of mental stress and injury.**

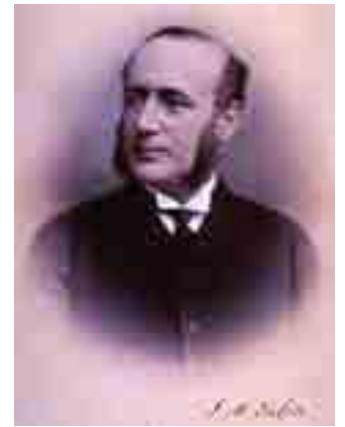
Dr. Silas Weir Mitchell, a Philadelphia based neurologist and novelist, co-authors the book *Gunshot Wounds and Other Injuries of Nerves*, an influential early text on nerve injuries. Eight years later Mitchell publishes a more comprehensive study entitled [Injuries of Nerves and Their Consequences](#). Many of Mitchell's conclusions are drawn from his observations as an Army surgeon during the Civil War. Considered together, his two works represent some of the most important early writings on the subject of neurology published in the United States. Mitchell is often referred to as the "Father of Neurology."



Dr. Silas Weir Mitchell. National Library of Medicine photo

1871

Philadelphia based surgeon and teacher Jacob Mendez Da Costa publishes the first study of Civil War era soldiers who experienced **unexplained mental and physical symptoms**, including shortness of breath, chest pain, fatigue, and a severe form of "homesickness." Da Costa labeled the disorder "irritable heart," but it would also become known as "Da Costa's Syndrome," "**soldier's heart**," the "effect syndrome," and "neurocirculatory asthenia." Da Costa attributes his patients suffering to a variety of factors related to the difficult living conditions experienced by soldiers, including infectious disease (48 percent) and strenuous activity (35 percent). He reports treating his patients with a combination of drugs, including opium, cannabis indica, and strychnine. However, mostly, he prescribed rest and reports that many of his patients, almost 40 percent, did eventually return to active duty.



Dr. Jacob Mendez Da Costa. National Library of Medicine photo

# World War I

British neurologist Sir Gordon Homes builds on the work of Inouye and continues to develop insights about effects of occipital lesions on the basis of 2,000 cases he observed during the war.

1914 -1918

“**Shell Shock**” emerges as a catchall category encompassing victims of physical (concussive) as well as mental (psychogenic or emotional) trauma.



*Left: Gordon Holmes pictured with colleagues at Bologne in 1915. Click the image to access a 2007 article about Holmes in the journal Brain. Oxfordjournals.org courtesy photo*

1940

# World War II

American psychiatrist Abram Kardiner publishes *The Traumatic Neuroses of War* and suggests the term “physioneurosis” to describe a disorder to which he attributed both organic and psychogenic causes. Kardiner’s observations were based upon his observation and treatment of over 1,000 U.S. World War I veterans as a doctor at a New York Veterans Bureau hospital. Kardiner’s book and his emphasis on the environmental factors contributing to neuroses would come too late to influence U.S. policy in World War II, but would become highly influential after the war.

The U.S. military attempts to prevent **mental health** casualties with more rigid **screening**. A strict program is instituted by psychiatrist Henry Sullivan Stack. However, the program is subsequently faulted for precipitating a manpower crisis, as the number of rejections and psychiatric discharges skyrockets. In all, 1.6 million potential recruits are barred from service on mental health grounds (a rate 7.6 times greater than during the First World War). When the more stringent screening process did not reduce the number of breakdowns, another 438,000 soldiers are discharged because of psychological health concerns.

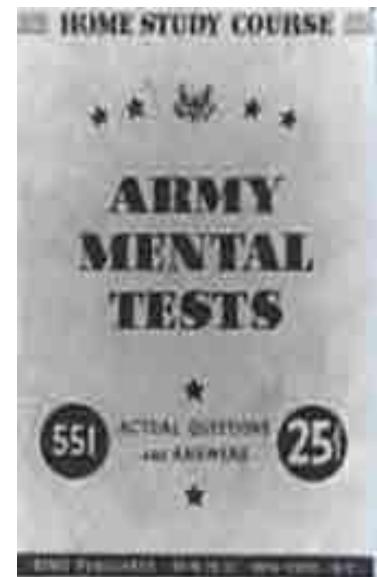


*Left: Potential air crew trainees complete one of several psychiatric screening tests used by the U.S. military during World War II.*

*Right: A booklet sold to help recruits prepare for the Army General Classification*



*Injured American troops at Omaha Beach await evacuation. National Archives and Records Archive photo*

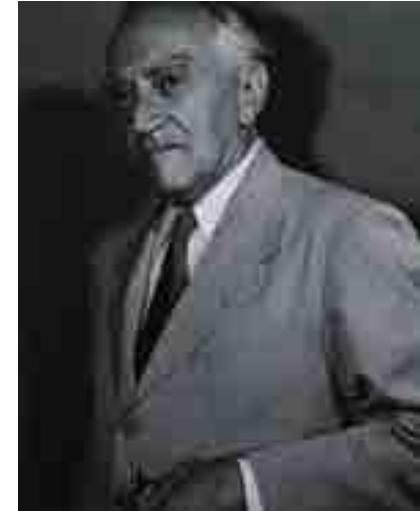


1942

The well known German neurologist and psychiatrist Dr. Kurt Goldstein publishes the first major English language version of his work on **traumatic brain injuries sustained in war**. As the director of the Institute for Research into the Effects of Brain Lesions and of the Frankfurt Neurological Institute, Goldstein worked with colleagues to pioneer new treatment and rehabilitation methods for brain injury patients from the First World War.

Goldstein's status as a prominent physician combined with the growing fame of his rehabilitation program at Berlin Moabit soon became a target of German anti-semitism. When the Nazi's seized power in 1933, he refused to abandon his patients, despite the evident personal risk involved, and was subsequently imprisoned and tortured. Friends eventually secured his release, but only after he pledged to leave Germany forever..

In 1941, Goldstein made his way to the United States, where he would spend the rest of his career. In 1942, an English language collection of his research from the last two decades was published as ***Aftereffects of Brain Injuries In War: Their Evaluation and Treatment***. The book contained Goldstein's observation of some two thousand patients, a group of whom he had chanced to observe and treat continually for almost two decades.



The German born neuropsychologist Dr. Kurt Goldstein. National Library of Medicine photo



1943

The possibility of a significant manpower shortage in the U.S. Army deepens as **psychiatric discharges exceed the total number of new enlistees** for the year, even as the demand for more recruits intensifies.

In November, newspapers in the United States report on an incident

in which U.S. Army **General George Patton slapped a “shell shocked” soldier**, leading to an investigation by military authorities.

Some historians point out that Patton’s actions may have been precipitated by his frustration with the ongoing manpower shortage, which many within the military traced back to the large numbers of neuropsychiatric discharges.

General George Marshall issues a memorandum in December 1943 criticizing the performance of military psychiatrists and blaming them for causing a manpower shortage. Marshall’s critique of military psychiatry leads to a change in policy and to the deployment of trained psychiatrists to the frontlines of the war in Europe and the Pacific.



General George Patton pictured in the first row, second from the left.  
Library of Congress photo



Left: Brig. Gen. Will Menniger, director of the neuropsychiatry consultants Division within the Office of the Surgeon General, 1943 to 30 June 1946. Army Medical Department photo

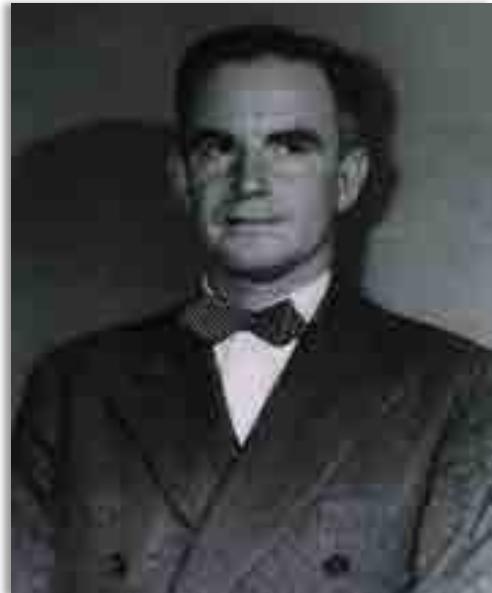
# Korea

Congress designates the National Institute of Neurological Disorders and Stroke (NINDS), an institute of the National Institutes of Health, to conduct and support research on brain and nervous system disorders.

## Mortality rates due to head injury during the Korean War continue to decrease.

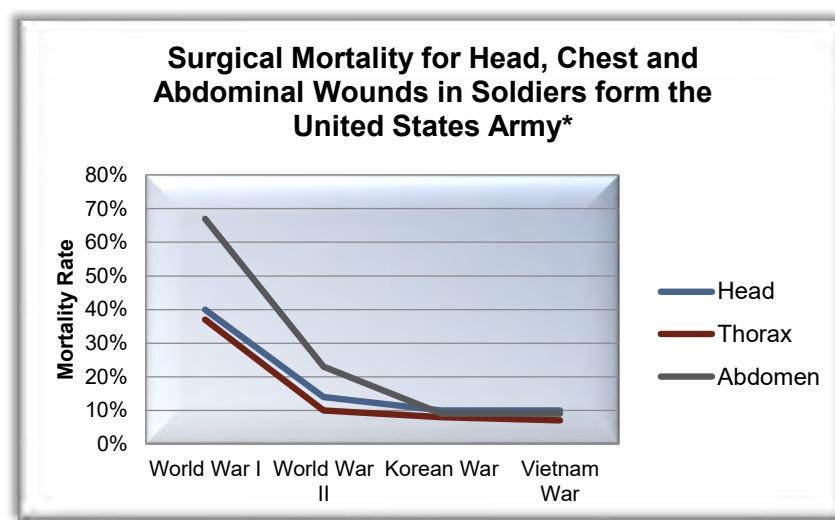
Division level teams are deployed to manage and evacuate hematoma cases rapidly from the battlefield. Improvements in care result in declining rates of menigocerebral infections to less than one percent by the end of the war.

1950 -  
1953



Right: Dr. William F. Caveness in 1949. National Library of Medicine photo

Dr. William Caveness initiates a study during the Korean War involving 407 Marine and Navy personnel with combat or combat support head injuries. The study divided patients into missile and non-missile cases and demonstrated a significant correlation between penetrating wounds and incidence of post-traumatic epilepsy. Between twenty and fifty-seven percent of those service members with penetrating head wounds experienced epilepsy.



Source: Trunkey, D. M. (2000). "History and Development of Trauma Care in the United States." *Clinical Orthopaedics* 374 (May): 36-46.



*Dr. Alex Luria with a patient  
in the 1960s. [luria.ucsd.edu](#)  
photo*

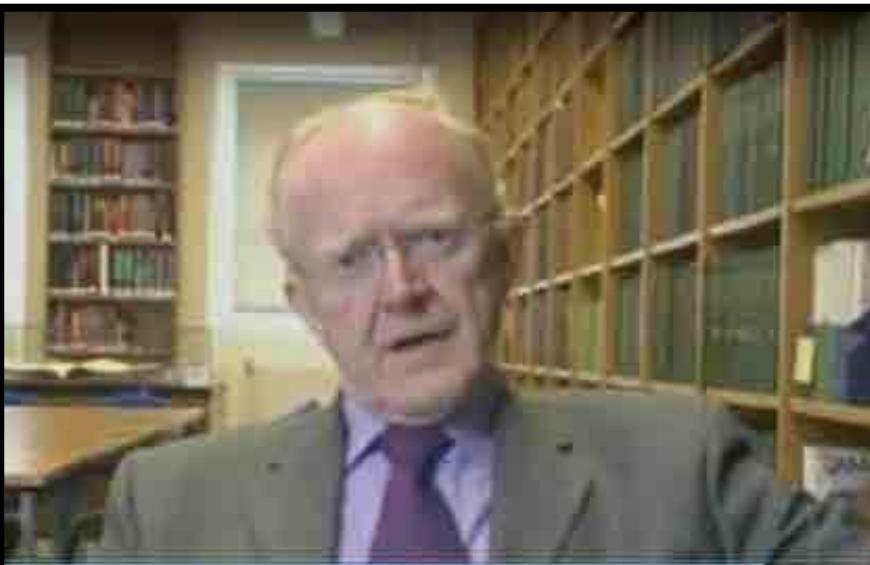
1960 –  
1974

# Vietnam

In the Soviet Union, Aleksandr Luria establishes many of the basic methods of head injury rehabilitation, some of which are still used today. Luria was also a major contributor to the establishment of neuropsychology. Luria based much of his work on his observation and treatment of soldiers and civilians with brain injuries during World War II.

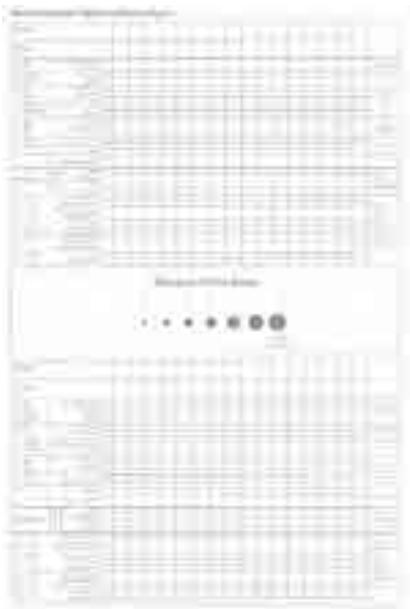
The National Institute of Health (NIH) begins Phase I of a Vietnam Head Injury Study examining the progress of 700 Vietnam veterans recovering from penetrating head trauma, directed by Dr. William Caveness.

Researchers (Graham Teasdale and Bryan J. Jennett) working at the University of Glasgow Institute of Neurological Sciences develop the fifteen point Glasgow Coma Scale (GCS) for measuring the effect of brain injuries. The GCS assigns a value to cognitive functions in three key areas: motor response, verbal response, and eye opening. It is one of several such tools used today to measure the impact of traumatic brain injuries.



*Above: An example of a patient chart  
based upon the GCS assessment scale.  
University of Glasgow photo*

*Left: Dr. Graham Teasdale, co-creator of  
the GCS. Additional resources about the  
history of the GCS can be found at the  
University of Glasgow [website](#). University  
of Glasgow photo*



1992

# Persian Gulf War

During the Persian Gulf War, **brain injuries accounted for seventeen percent of all casualties.** The SCUD missile attacks conducted by the Iraqi military during the war draw increased attention to head and neck injuries.

1993

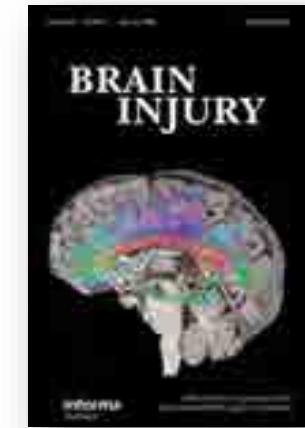
The Defense and Veterans Head Injury Program (DVHIP) is established by Congress to respond to the need for standardized traumatic brain injury treatment and rehabilitative services among military service members and veterans. Later renamed the Defense and Veterans Brain Injury Center or DVBIC, the DVHIP is designed as a collaborative effort between the Department of Defense and the Department of Veterans Affairs. DVBIC headquarters were located at Walter Reed Army Medical Center until August 2011.

DVBIC sponsors the first [randomized control study](#) of TBI rehabilitation therapy in the United States in collaboration with the VA at Hospitals and Medical Centers in Minnesota, Florida, California, and Virginia.

1996

The [International Brain Injury Association \(IBIA\)](#) is founded to “encourage international exchange of information, to support research, to provide training especially in developing countries and to advocate for brain injury.”

Congress passes the **Traumatic Brain Injury Act of 1996** “to amend the Public Health Service Act to provide for the conduct of expanded studies and the establishment of innovative programs with respect to traumatic brain injury.” Also known as Public Law 104-166, it leads to expansion of TBI surveillance systems at the state level. Three years later the Center for Disease Control’s National Center for Injury Prevention and Control produced the first [report](#) about the impact of TBI in the United States as required by the 1996 legislation.



Left: Brain Injury is the official journal of the IBIA. Click the image to learn more. IBIA photo

1998

NIH convenes the Consensus Development Conference on Rehabilitation of Persons with Traumatic Brain Injury, resulting in a **Consensus Statement on TBI Rehabilitation**. Among the conclusions reached by a 16 member panel of specialist examining the available data is recognition of the increasing numbers of TBI cases across the country. The increase is largely attributed to better emergency care. The panel also notes that there is a need for more studies and research to evaluate rehabilitation therapy.

1999

The National Centers for Injury Prevention and Control, a division of the Center for Disease Control, issues its first report to Congress on mild traumatic brain injury or mTBI in the U.S.

# OEF and OIF

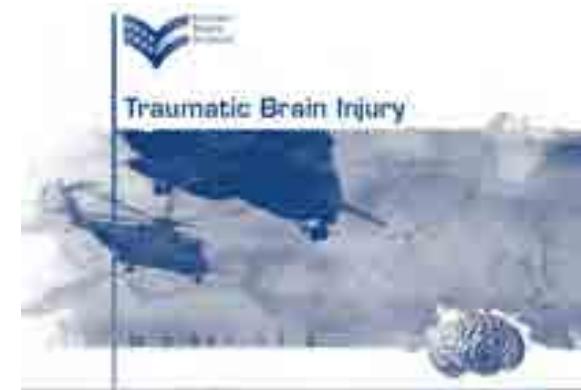
The beginning of Operation Enduring Freedom in 2001, followed in 2003 by Operation Iraqi Freedom.

**Veterans Health Initiative (VHI) on TBI** is released by DVBIC and the Department of Veterans Affairs in 2004.

2001-  
2004

Congress allocates funding to support VA care and rehabilitation through the Veterans Health Programs Improvement Act.

The Army Medical Research and Materiel Command initiates Phase III of the Vietnam Head Injury Study, completed in 2007.



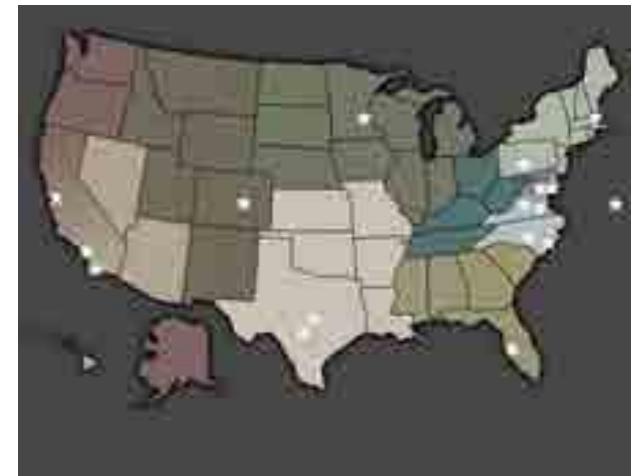
*The VA released a Veterans Health Initiative study guide to help train health care providers who care for Veteran patients with TBI. Click the image above to learn more and to access the study guide. Department of Veterans Affairs photo*

2005

DVBIC adds 4 Polytrauma Rehabilitation Centers and 21 Polytrauma sites to its network of providers and partnerships that care for the combat wounded. Between 2005 and 2011 over 2,000 veterans with a TBI received care at a VA Trauma Rehabilitation Center.

At the same time, in April of 2005 the VA establishes the **TBI Polytrauma System of Care** encompassing over 100 VA facilities. The DVBIC centers and sites are part of this larger Polytrauma Network. Over 32,000 veterans received care at TBI Polytrauma Network sites between 2005 and 2011.

DVBIC's network of cities and regional partnerships extends TBI care to remote, often underserved locations around the country and the globe.



*Click the image above to access DVBIC's interactive map of regional coordinators and partners. DVBIC photo*

2005

The Assistant Secretary of Defense (Health Affairs) mandates the Post-Deployment Health Reassessment (PDHRA) requiring a second mental health assessment 3-6 months after return from deployment. The PDHRA uses DD Form 2900 to track health concerns, assessments, and referrals for all active duty service members, National Guard and Reserve members. The DD Form 2900 has since been updated to better screen for a variety of mental health conditions as well as TBI.

The [Center for Deployment Psychology \(CDP\)](#) is created with a mandate from Congress.

2006



DoD Task Force on Mental Health created via Section 723 of the National Defense Authorization Act FY 2006.

DVBIC develops the [Military Acute Concussion Evaluation \(MACE\)](#), a screening tool allowing front line providers to quickly measure cognitive functions in four key areas: orientation, immediate memory, concentration, and memory recall. This information can be combined with other clinical data to make determinations about treatment and care.

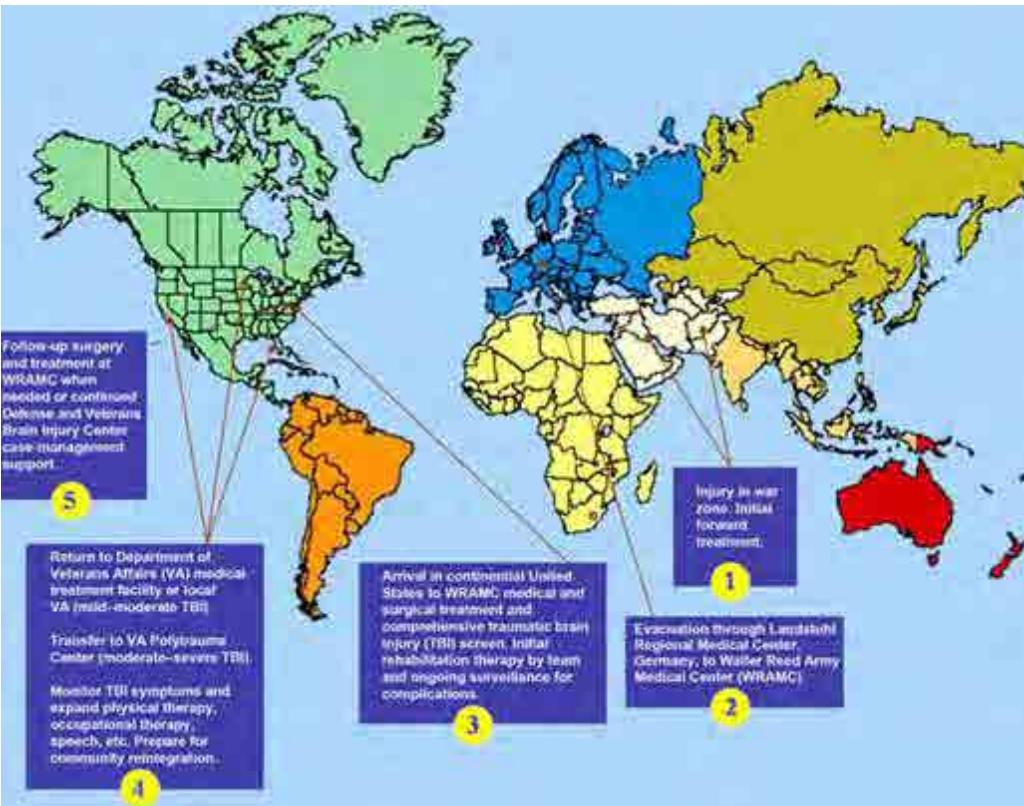
*DD Form 2900*

MACE

The VA Polytrauma Telehealth Network is established in December 2006 to link and improve communication between VA rehabilitation facilities.

2006

DVBIC develops the [Military Acute Concussion Evaluation \(MACE\)](#), a screening tool allowing front line providers to quickly measure cognitive functions in four key areas: orientation, immediate memory, concentration, and memory recall. This information can be combined with other clinical data to make determinations about treatment and care.



Lt. Col. (Dr.) Margaret Swanberg performs a MACE demonstration at Forward Operating Base Hammer, Iraq, July 18, 2008. U.S. Army photo.

*Left: Using interactive video teleconferencing doctors treating TBI patients in theater can consult with experts located in the United States. Between 2005 and 2011, there were over 775 telehealth encounters involving treatment or screening for TBI. VA Journal of Rehabilitation Research photo*

MILITARY ACUTE CONCUSSION EVALUATION TOOL

Initial Assessment

1. Name \_\_\_\_\_  
2. Date \_\_\_\_\_  
3. Age \_\_\_\_\_  
4. Sex \_\_\_\_\_  
5. Injury Type \_\_\_\_\_  
6. Injury Mechanism \_\_\_\_\_  
7. Injury Location \_\_\_\_\_  
8. Injury Severity \_\_\_\_\_  
9. Injury Date \_\_\_\_\_  
10. Injury Time \_\_\_\_\_  
11. Injury Duration \_\_\_\_\_  
12. Injury Description \_\_\_\_\_  
13. Injury Diagnosis \_\_\_\_\_  
14. Injury Treatment \_\_\_\_\_  
15. Injury Complications \_\_\_\_\_  
16. Injury Recovery \_\_\_\_\_  
17. Injury Rehabilitation \_\_\_\_\_  
18. Injury Prognosis \_\_\_\_\_  
19. Injury Follow-up \_\_\_\_\_  
20. Injury Notes \_\_\_\_\_

*Right: Click the image to access a copy of the MACE template.*

San Antonio becomes the fifth Polytrauma Rehabilitation Center location.

The TBI Second Level Evaluation template is issued to evaluate returning OEF and OIF veterans who screened positive on all four questions of the primary TBI screening tool contained in the VA Computerized Patient Record System or who were previously diagnosed. The template integrates with the Traumatic Brain Injury Registry.

DVBIC becomes the primary operational TBI component for the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury.

2007



*Senator Kay Bailey Hutchison (center) speaks with U.S. Army Spc. (retired) Chris Harmon and his mother at the dedication of the San Antonio Polytrauma Rehabilitation Center. Also in attendance, Secretary of Veteran Affairs Eric K. Shinseki (right). Photo by Bob Owen courtesy of San Antonio Express News*

2008

DVBIC designated as the Office of Responsibility for the Neurocognitive Assessment Tool Program. The NCAT builds on existing DoD protocols such as the [Military Acute Concussion Evaluation](#) MACE and [Army Automated Neuropsychological Assessment Metric](#) (ANAM) with the purpose of gathering data before and after service members are exposed to a blast event to improve mTBI screening, diagnosis and treatment.



One quarter of all service members evacuated from Iraq and Afghanistan are reported to have head and neck injuries.

Right: An NCAT Information Sheet published on the Defense Health Information Management System (DHIMS) website.

Left: DHIMS homepage. DHIMS photo

#### Neurocognitive Assessment Tool (NCAT) Information Sheet

The Department of Defense is taking another step forward in the charge to better screen for, diagnose and treat mild traumatic brain injury (mTBI).

DoD requires pre-deployment Neurocognitive Assessment Tools (NCATs) for all Service members prior to their next deployment. NCATs measure cognitive performance, memory, and skills affected by blast, including cognition, memory, and thinking ability. A Service member will serve as a baseline in monitoring changes in a Service member's cognitive function. Ultimately, the goal is to have the capability to compare assessment results before and after a Service member is subject to a blast event, in order to improve the accuracy of mTBI screening and protect the health of Service members.

"Following a concussion or mTBI, Service members are evaluated for physical findings, reported symptoms and alterations in cognition. In most cases, individuals recover from the effects of concussion or mTBI," said Robert L. Kane, Ph.D., Army Pic, Director of the NCAT Program. "However, physical signs, symptoms and cognition may not recover at the same rate. The Automated Neuropsychological Assessment Metrics provides an additional tool to assess cognitive changes following concussion or mTBI and to assess improvement."

NCATs are important because Service members involved in a blast may have no visible external injuries and the symptoms of mTBI can go unnoticed. These symptoms may include slower reaction time, headaches, irritability, memory impairments and sleep difficulty.

The Automated Neuropsychological Assessment Metrics (ANAM) is the specific type of NCAT that Service members will complete. It is a simple 15 to 30 minute computerized test that records a Service member's cognitive performance. The Army began developing the ANAM in 1996. It was validated and refined for a number of uses over the last two decades, most notably for publications involving the 101st Airborne Division.

"ANAM contributes to the general assessment of the effects of concussion or mTBI and to monitoring the course of recovery," Kane said. "It is a tool that helps in the determination of appropriate follow-up care and readiness to return to duty."

The ANAM on its own is not a diagnostic tool. It does not measure attention or cognitive skills. The changes in cognitive function revealed by assessment will trigger a more in-depth evaluation by a medical provider. Preliminary data from pre-deployment cognitive assessments has shown the number of these kinds of referrals to be very low.

ANAM results will be a part of Service members' medical records. This data will be treated as protected personal health information and kept confidential using encryption technology.

As of 2009, blast related injuries (i.e. from improvised explosive devices or IEDs, land mines, rockets, shrapnel, etc.) account for over 60 percent of combat injuries in OEF and OIF. Of those injured in a blast related incident, 65 percent have symptoms of traumatic brain injury.

# January 18, 2007

The New York Times

PRO FOOTBALL

## Expert Ties Ex-Player's Suicide to Brain Damage

By ALAN SCHWARZ JAN. 18, 2007

Since the former National Football League player Andre Waters killed himself in November, an explanation for his suicide has remained a mystery. But after examining remains of Mr. Waters's brain, a neuropathologist in Pittsburgh is claiming that Mr. Waters had sustained brain damage from playing football and he says that led to his depression and ultimate death.

The neuropathologist, Dr. Bennet Omalu of the University of Pittsburgh, a leading expert in forensic pathology, determined that Mr. Waters's brain tissue had degenerated into that of an 85-year-old man with similar characteristics as those of early-stage Alzheimer's victims. Dr. Omalu said he believed that the damage was either caused or drastically expedited by successive concussions Mr. Waters, 44, had sustained playing football.



In a telephone interview, Dr. Omalu said that brain trauma "is the significant contributory factor" to Mr. Waters's brain damage, "no matter how you look at it, distort it, bend it. It's the significant forensic factor given the global scenario."

He added that although he planned further investigation, the depression that family members recalled Mr. Waters exhibiting in his final years was almost certainly exacerbated, if not caused, by the state of his brain — and that if he had lived, within 10 or 15 years "Andre Waters would have been fully incapacitated."

Dr. Omalu's claims of Mr. Waters's brain deterioration — which have not been corroborated or reviewed — add to the mounting scientific debate over whether victims of multiple concussions, and specifically longtime N.F.L. players who may or may not know their full history of brain trauma, are at heightened risk of depression, dementia and suicide as early as midlife.

The N.F.L. declined to comment on Mr. Waters's case specifically. A member of the league's mild traumatic brain injury committee, Dr. Andrew Tucker, said that the N.F.L. was beginning a study of retired players later this year to examine the more general issue of football concussions and subsequent depression.

Eagles safety Andre Waters making a tackle in 1988. Waters had a reputation as one of football's hardest-hitting defensive players. Credit Al Messerschmidt/WireImage

# February 18, 2007

**Pulitzer Prizes**



**JOURNALISM — Public Service**

**The Washington Post**

## Soldiers Face Neglect, Frustration At Army's Top Medical Facility

By Dana Priest and Anne Hull  
Washington Post Staff Writers

February 18, 2007; Page A17

Behind the door of Army Spec. Jeremy Duncan's room, part of the wall is torn and hangs in the air, weighted down with black mud. When the wounded combat engineer stands in his shower and looks up, he can see the bathtub on the floor above through a cattail hole. The stone building, constructed during the world war, often smells like grass, carry-out. Signs of neglect are everywhere: mouse droppings, oily oil cockroaches, stained carpets, cheap mattresses.

This is the world of Building 18, not the kind of place where Duncan expected to recover when he was evacuated to Walter Reed Army Medical Center from Iraq last February with a broken neck and a shredded left ear, nearly dead from blood loss. But the old lodge, just outside the gates of the hospital and five miles up the road from the White House, has housed hundreds of maimed soldiers recuperating from injuries suffered in the wars in Iraq and Afghanistan.

The common perception of Walter Reed is of a singular hospital that shines as the crown jewel of military medicine. But 5 1/2 years of sustained conflict have transformed the venerable 133-acre institution into something else entirely — a holding ground for physically and psychologically damaged outpatients. Among 709 of them — the majority soldiers, with some Marines — have been released from hospital beds but still need treatment or are awaiting irreversible decisions before being discharged or returning to active duty.

They suffer from brain injuries, severed arms and legs, organ and back damage, and various degrees of post-traumatic stress. Their legions have grown exponentially — they outnumber hospital patients at Walter Reed 17 to 1 — that they take up every available bed in post and spill into dozens of nearby hotels and apartments leased by the Army. The average stay is 12 months, but some have been stuck

**Photo caption:** In the shower in Building 18, Spec. Jeremy Duncan, 21, a combat engineer, stands in water that has leaked through a hole in the ceiling. He was evacuated from Iraq with a broken neck and a shredded ear.

there for as long as two years.

Not all of this suffering are as bleak as Duncan's, but the shadow of Building 18 symbolizes a larger problem in Walter Reed's treatment of the wounded. According to dozens of soldiers, family members, veterans aid groups, and current and former Walter Reed staff members interviewed by two Washington Post reporters, who spent more than four months visiting the sprawling ward without the knowledge or permission of Walter Reed officials, many agreed to be quoted by name; others said they feared Army retribution if they complained publicly.

While the hospital is a place of scrubbed-down order and duly intrepid, with medical advances saving more soldiers than ever, the outpatients in the Other World Ward encounter a messy bureaucracy, battered wards as chaotic as the war-tattered ones they faced overseas.

On the warm days, soldiers say their feet feel like they are living a chapter of "Catch-22." The wounded manage other wounded. Soldiers dealing with psychological disorders of their own have been put in charge of others at risk of suicide.

Dilengaged cooks, unqualified platoon sergeants and overworked case managers fumble with simple needs: finding soldiers' families who are close to poverty, replacing a uniform ripped off by rebels in the desert sand or helping a brain-damaged soldier remember his next appointment.



"We've done our duty. We fought the war. We came home wounded. True. But whenever the people are back home who are supposed to give us the easy transition should be doing it," said Marine Sgt. Ryan Groves, 26, an amputee who lived at Walter Reed for 16 months. "We don't know what to do. The people who are supposed to know don't have the answers. It's a hellish process of waiting."

Soldiers, family members, volunteers and caregivers who have tried to fix the system say such mishaps seem fixed by itself, but the cumulative effect weakens trust in the safety of the wounded and can stall their recovery.

"It creates inaction and disengagement," said Joe Wilson, a clinical social worker at Walter Reed. "These soldiers will withdraw and stay in their rooms. They will actively avoid the very treatment and services that are

meant to be helpful."

Darwin Scott, a hospital liaison officer for Operation Enduring Freedom who helps discharge 125 wounded service members each week at Walter Reed, said soldiers "get awesome medical care and their lives are being saved." But, "Then they get into the administrative part of it, and they are like, 'You saved me for what?' The soldiers feel like they are not getting proper respect. This messes things up."

This world is invisible to outsiders. Walter Reed occasionally showcases the heroism of those wounded soldiers and emphasizes that all is well under the circumstances. President Bush, former defense secretary Donald H. Rumsfeld and members of Congress have promised the best care during their regular visits to the hospital's soft-polished impulse unit, Ward 5-2. "You owe them [the] care you give them," Bush said during his last visit, a few days before Christmas. "Not only for when they're in harm's way, but when they come home to help them adjust if they have wounds, or help them adjust after that time in service."

Along with the government promises, the American public, determined not to repeat the divisive Vietnam experience, has embraced the soldiers even as the war grows more controversial at home. Walter Reed is awash in the generosity of volunteers, businesses and celebrities who donate money, plane tickets, telephone bills and steak dinners.

Yet at a deeper level, the soldiers say they feel alone and frustrated. Seventy-five percent of the troops polled by Walter Reed last March said their experience was "stressful." Suicide attempts and understandings override prescription drugs and alcohol, which is sold on post, are just part of the narrative here.

Vera Heron spent 13 frustrating months living on post to help care for her son. "It just absolutely took forever to get anything done," Heron said. "They do the paperwork, then into the paperwork. Then they have to redo the paperwork. You are talking about days and

# Psychological Health and Traumatic Brain Injury Congressional Special Appropriations

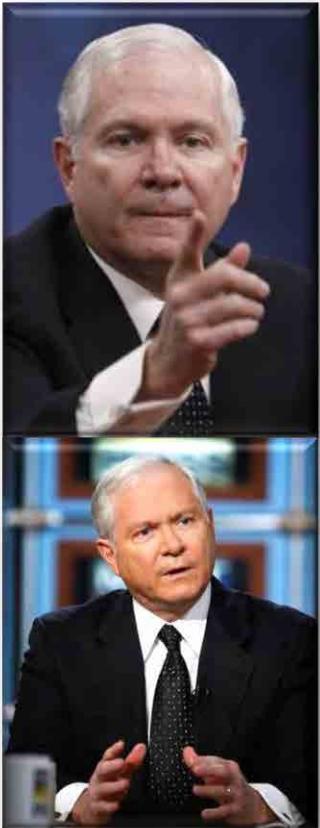
Fiscal Year	Amount
2007	\$300m
2009	\$90m
2009	\$75m
2010	\$120m
2011	\$100m
2012	\$135m
2013	\$135m
2014	\$125m
2015	\$120m
2016	\$120m
2017	\$125m
2018	\$125m
2019	\$125m

(+ \$600m to improve care for Psychological Health and TBI in 2007)

In addition to Service Program funds, CNRM funding, DVBIC funding, End-of-year funds, etc.

# CHANGE DRIVERS FOR THE MILITARY MEDICAL RDA MISSION

## Secretary of Defense Guidance



**June 26, 2008**

### Secretary Gates Memorandum *Caring for Our Wounded Personnel and Their Families*

"I request the development of a tailored plan to provide R&D investments that advance state of the art solutions for world class medical care with an emphasis on Post Traumatic Stress Disorder, Traumatic Brain Injury, prosthetics, Restoration Sight Eye-Care, and other conditions directly relevant to the injuries our soldiers are currently receiving on the battlefield."

**April 6, 2009**

### Secretary Gates News Conference

#### *Details New Pentagon Priorities*

FY2010 Defense Budget: "Continue the steady growth in medical research and development by requesting \$400 million more than last year."



## Secretary of the Army Imperatives

### SUSTAIN

- ✚ Sustain Soldiers, Civilians and Families, through recruiting and improving quality of life
- ✚ Taking care of wounded Soldiers
- ✚ Rehabilitate Soldiers and get them back into the fight



### PREPARE

- ✚ To continue to prepare Soldiers for success in the current conflict
- ✚ Continue to adapt its training and equipment to keep ahead of an adaptive enemy
- ✚ Training leaders and Soldiers



### RESET

- ✚ Continue to reset units and to rebuild the readiness consumed in operations, to prepare them for deployments and future contingencies
- ✚ Reset for the future, not the past

### TRANSFORM

- ✚ Transform the Army to meet the demands of the 21<sup>st</sup> century
- ✚ Continually modernize our forces and put our Cold War formations and systems behind us
- ✚ Future Combat Systems research and development is currently the Army's largest effort to modernize

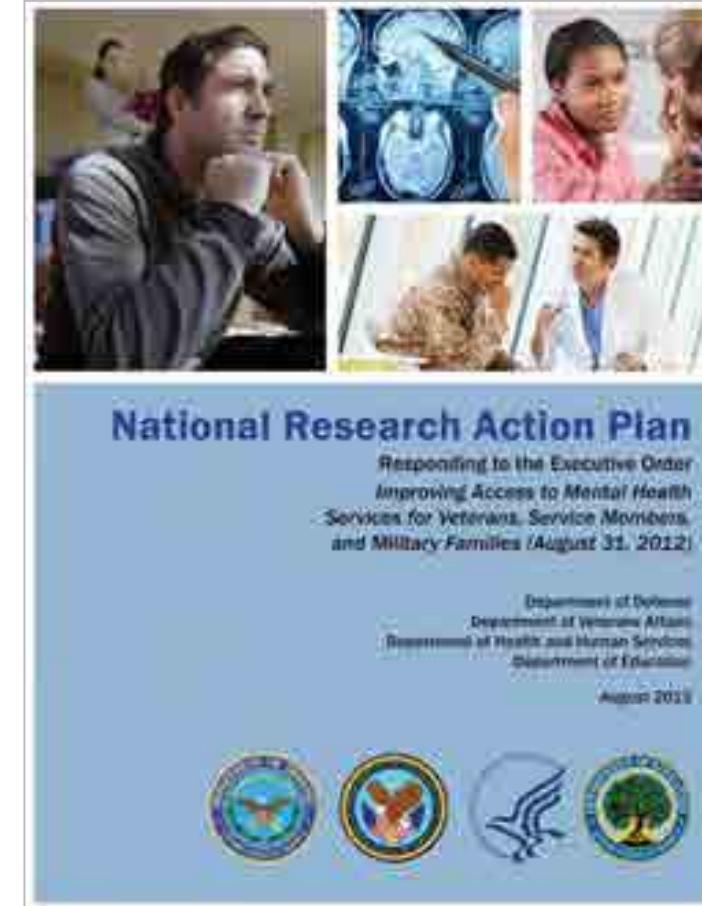
# **Presidential Executive Order 31 Aug 2012: Improving Health Care for Veterans, Service Members, and Military Families Affected by . . . TBI**

## **Sec. 5. Improved Research and Development**

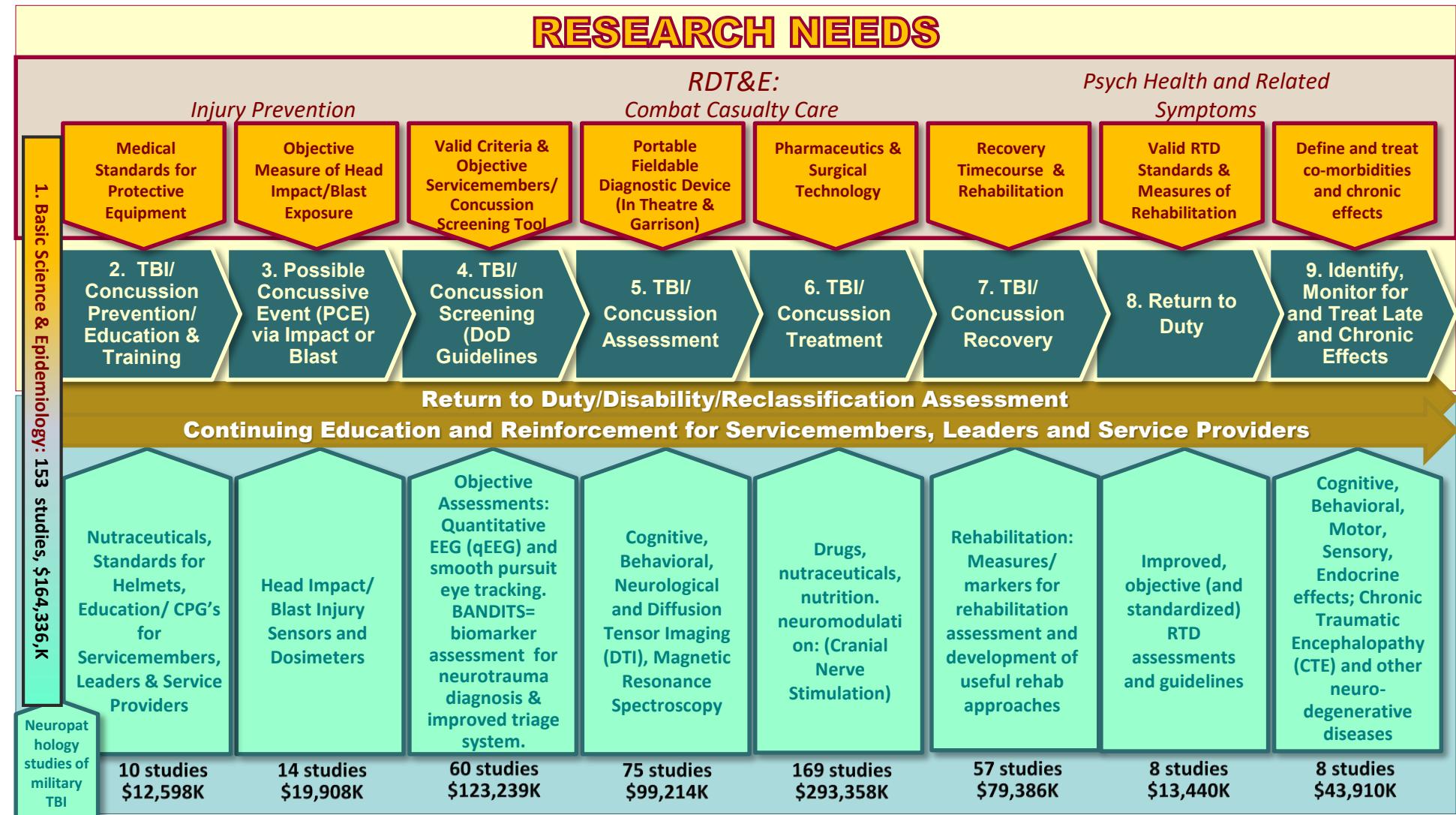
- DoD, VA, HHS, and Dept of Ed in coordination with the Office of Science and Technology Policy shall establish a National Research Action Plan within 8 months of the date of this order to improve the coordination of agency research of TBI, PTSD, and other mental health conditions to reduce the number of affected men and women through better prevention, diagnosis, and treatment.
- **National Research Action Plan shall:**
  - Establish strategies to establish surrogate and clinically actionable biomarkers for early diagnosis and treatment effectiveness
  - Develop improved diagnostic criteria for TBI
  - Enhance understanding of mechanisms responsible for PTSD, related injuries, and neurological disorders following TBI
  - Foster development of new treatments for these conditions based on better understanding of underlying mechanisms
  - Improve data sharing between agencies and academic and industry researchers to accelerate progress and reduce redundant efforts without compromising privacy
  - Make better use of electronic health records to gain insight into the risk and mitigation of PTSD, TBI, and related injuries
  - Include strategies to support collaborative research to address suicide prevention

# National Research Action Plan

- Response to President Obama's 2012 Executive Order
- Interagency Collaboration:
  - DoD, VA, HHS, NIDRR (Dept of Education)
- Key Themes Specific to TBI Research:
  - Biomarkers: (Imaging, proteomic, neurophysiologic, etc.) to diagnose and monitor recovery
  - Diagnosis: more precise classification system, personalized/targeted diagnosis
  - Mechanisms: increase understanding of neuropathology
  - Treatment: identify and validate pharmacologic and rehabilitation treatment options



# Continuum of TBI Care Determines Research Approach

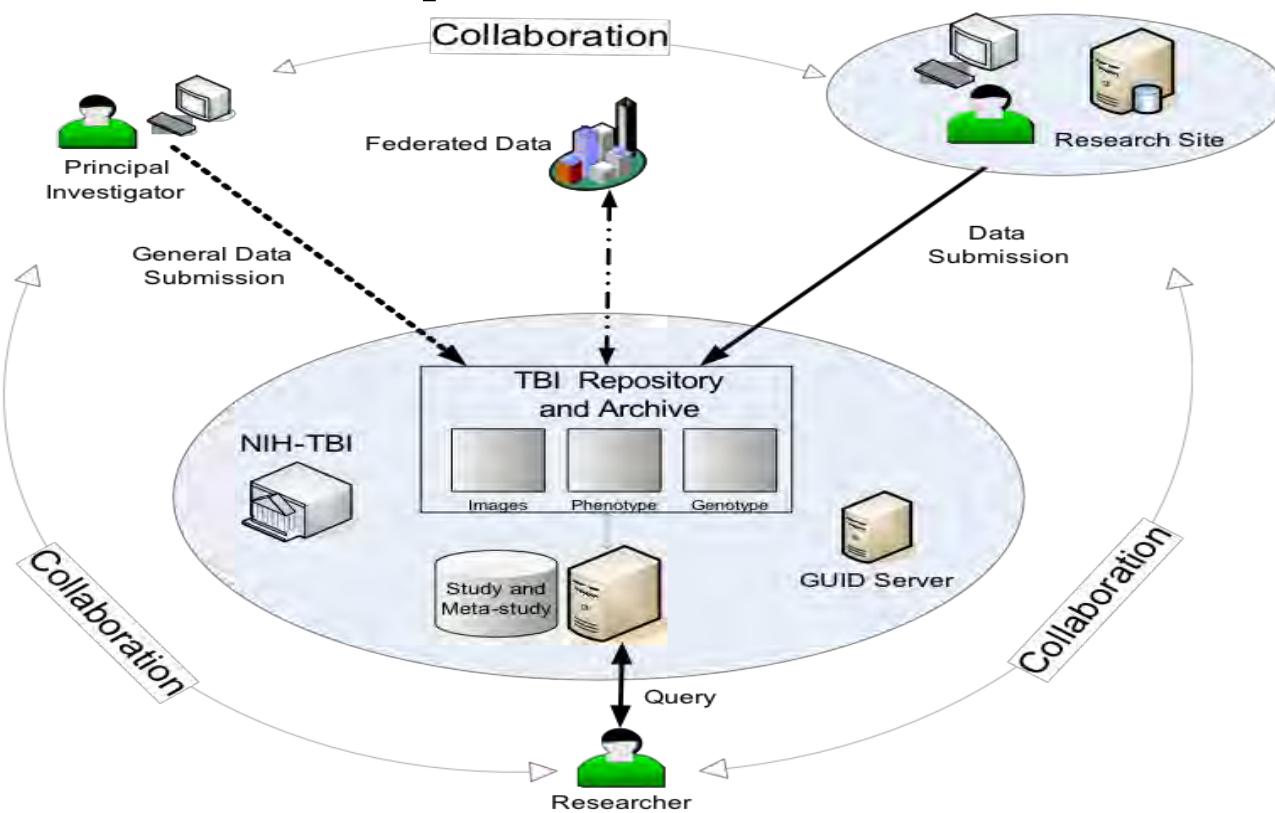


Updated 4 March 2015

# FITBIR Data Repository: Federal Interagency TBI Research

*A collaboration between NIH and DoD to develop a biomedical informatics system to accelerate scientific discovery and treatment in Traumatic Brain Injury*

## Database with multiple contributors and multiple accessors



# Assessment of Head Injury in the Emergency Department: Clinical Validation of the BrainScope® Ahead™ M-100, 200, 300

## Study/Product Aim(s):

- Demonstrate the ability to classify patients suspected of a brain injury (3 categories of severity)
- Demonstrate the ability to classify patients by providing gradations of functional brain injury
- Demonstrate better ability than the New Orleans Criteria decision rule for obtaining a CT scan
- Demonstrate that the proportion of subjects classified into Category 3 is greater than for Category 2



May 4th, 2011 – BrainScope® Company, Inc. today announced that it has reached concurrence with the U.S. Food and Drug Administration (FDA) on the key study design elements for clinical validation of the Ahead™ M-100 medical device. BrainScope's Ahead™ M-100 is being developed to address the unmet need for a medical device to aid in triage of patients with suspected TBI.

Activities FY	11	12	13
MS 1: Negotiate/finalize IRB/CRO/study agreements			
MS 2: First/last pt. enrolled into the trial			
MS 3: Data Analysis and Final Report			
MS 4: FDA Marketing Application Submitted			

## Goals/Milestones:

### FY11 Goals

- Establish infra-structure Contract Research Organization, Institutional Review Board protocol, Finalize agreements with participating hospitals. Begin study enrollment

### FY12 Goals

- Complete data acquisition, develop a fully integrated clinical study report in accordance with ICH GCP 1.13

### FY13 Goals

- Complete pivotal trial

### FY14 Goals

- Receive FDA Clearance as an indicator of a positive CT Scan

## Comments/Challenges/Issues/Concerns

- First patient enrolled August 2012
- PI redesigned device 7 times in response to issues encountered
- Several publications demonstrating utility in sports concussion and F/U
- Pivotal Trial completed, Submission and resubmission process for clearance by FDA > 1 yr

# Biomarker Assessment for Neurotrauma Diagnosis & Improved Triage System (BANDITS)

## Study/Product Aim(s)

- Minimal- to non-invasive medical device to identify and assess internal brain injuries
- State-of-the-art lightweight, sturdy and reliable diagnostic systems appropriate for far forward screening, assessment, and care
- Designed to diagnose mild, moderate and severe traumatic brain injury



## Approach

The goal of the BANDITS program is to develop a blood test for brain cell damage (much like the current blood test (Troponin) for heart damage).

BANDITS will be embedded in an automated system available to Level III or lower echelons of care from a open benchtop system to a handheld device.

- Pilot study = first in human experience to determine if it is possible to detect markers
- Feasibility study = explore the biomarker validity in applicable patient population and generate data to establish diagnostic claims
- Pivotal study = satisfy clinical regulatory requirements needed to support premarket authorization by FDA by production of results to confirm the diagnostic claims

## Handheld Device Role 1 (future)



### Goals/Milestones

#### FY11 Goals –

- Complete pilot study in mild and moderate TBI subjects
- Complete feasibility study in severe TBI subjects

#### FY12 Goals –

- Finalize the development of the benchtop system for the pivotal trial
- Begin Pivotal trial for mild-moderate and severe TBI subjects

#### FY14 Goals –

- Conclude pivotal trial

#### FY15 Goals –

- Submit PMA package to the FDA for the approval of TBI assay systemdevelopment

FDA Approved BTI 14Feb2018

# TBI Endpoints Development (TED)

## Study/Product Aim(s)

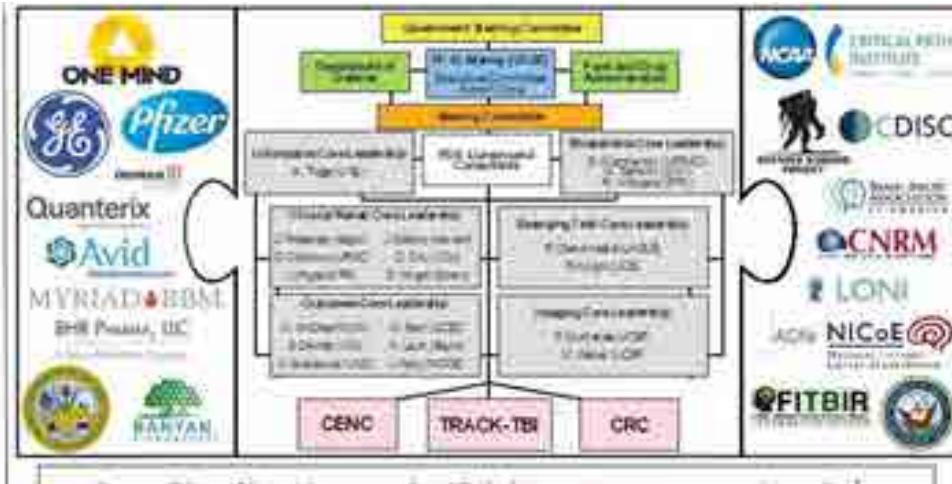
- OVERALL: Validate endpoints to improve clinical trial design to inform/accelerate FDA approval of TBI diagnostic tools and therapeutic agents
- Stage I: Identify candidate endpoints/surrogate markers for mTBI and modTBI across: TBI severity, spectrum of time, domains of function; Select 5 "seed projects" to demonstrate feasibility and reproducibility of promising prognostic and predictive properties; Convene 2 Consensus Conferences
- Stage II: Validate clinically relevant endpoints and surrogate markers identified during Phase I; Convene Implementation Conf.

## Approach

ID clinically relevant endpoints/surrogate markers using data-driven analytic approach; reach consensus via Delphi process to select most promising endpoints to validate in Stage II, based on their practical utility to support FDA approval. Collaborate with stakeholders to ensure implementation and dissemination.

## Timeline

Activities	CY	14	15	16	17	18
Integrate/Analyze TBI datasets						
Consensus Conferences 1 and 2						
Conduct Validation studies						
Implementation Conference						



Our coalition of investigators and public/private partners represent the nation's leading TBI innovators. Leadership and recruited Core expertise will produce deliverables predicted to improve care and outcomes for all populations affected by TBI.

## Goals/Milestones

**CY14 Goals** – Consensus Conference 1; Integrate multiple TBI datasets; ID methodologies; Initiate contact with FDA

- Commence Expert Working Group and Core Analyses
- Publish Consensus Conference proceedings

**CY15 Goal** – Consensus Conference 2; TBE-CDEs in CDISC Standard

- Select Seed Demonstration/Feasibility Projects
- Prioritize and select measures for Stage 2 validation
- Launch FDA Qualification Process (Stages 1 and 2)
- Produce manuscripts for peer-reviewed journals

**CYS16-17 Goals** – Conduct Validation studies

- Produce manuscripts for peer-reviewed journals

**CY18 Goals** – Complete validation studies/Implementation Conference

- Roadmap for completion of FDA Qualification Process (Stage 3); Dissemination of TED lessons learned

# Chronic Effects of Neurotrauma

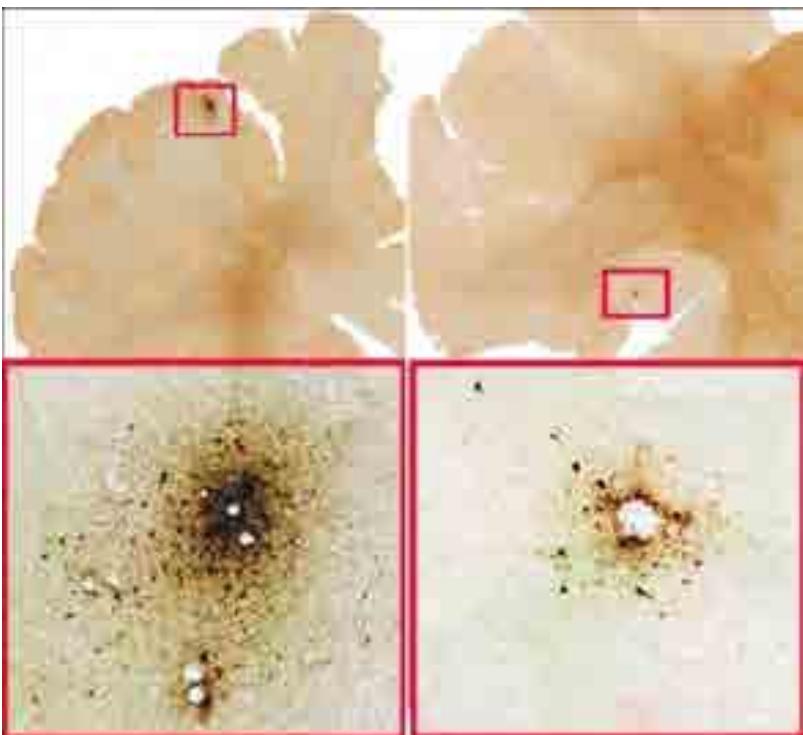
- Studies of boxers have demonstrated that repeated blows to the head can lead to Chronic Traumatic Encephalopathy (CTE)

**Stage I CTE: High school football player**

**Death at age 18 - 10 days after 4<sup>th</sup>  
concussion**

**Perivascular tau in frontal cortex**

- Dr Ann McKee, Boston VA. MHSRS 2012 Presentation



<https://cenc.rti.org/>

The mission of the CENC is to fill the gaps in knowledge about the basic science of mTBI (also termed concussion or mild TBI), determine its effects on late-life outcomes and neurodegeneration, identify Service members most susceptible to these effects, and identify the most effective treatment strategies. The CENC is a multi-center collaboration linking premier basic science, translational, and clinical neuroscience researchers from the DoD, VA, academic universities, and private research institutes to effectively address the scientific, diagnostic, and therapeutic ramifications of mTBI and its long-term effects.



# NCAA-DoD Grand Alliance Initiative

## Executive Committee

Leadership from NCAA (B. Hainline), DoD (D. Hack), NIH (W. Koroshetz)



### Concussion Research Initiative

#### Consortium (Operating Committee)

Co-Chairs:

Consortium Members selected from the Pac-12,  
Big 10, SEC, ACC, Big 12, and Ivy League  
conferences

Senior Scientific Advisory  
Board



### Educational Grand Challenge

#### Consortium (Operating Committee)

Nine Sigma: Beighley, Kacsandi, Resnick, Stark,  
Young; NCAA: Dunham, Hainline; DoD: Cozzarelli,  
Hack, Maxfield-Parker, Quinkert

Immediate Impact  
Challenge

Long-Term Impact  
Challenge

Advanced Research  
Coordinating Center



WR

Walter Reed  
Institute of Medicine

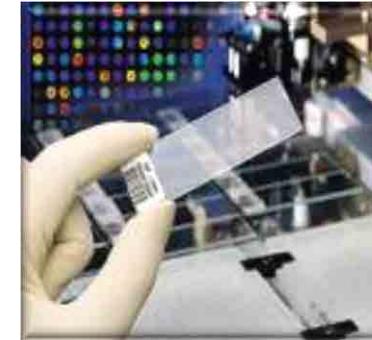
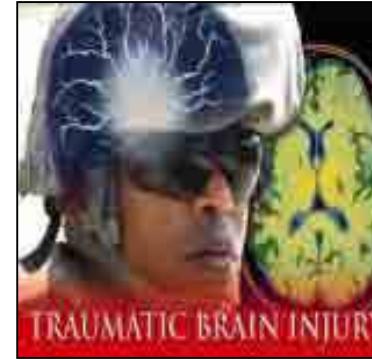


# Combat Casualty Care Research Program

## CCCRP Funds Distribution (CBE) /Program Plan Update Board of Director's Briefing



- COL Dallas Hack
- CCCR P Director
- 4 June 2014



# Numerous Entities Engaged in Military Related TBI Research

- WRAIR
- CNRM & Other USU Groups
- DVBIC
- NICoE
- Military TBI Clinics
- VA Programs
- Non-Profits
- & Many more



DEPUTY SECRETARY OF DEFENSE  
1010 DEFENSE PENTAGON  
WASHINGTON, DC 20301-1010

OCT - 1 2018

MEMORANDUM FOR CHIEF MANAGEMENT OFFICER OF THE DEPARTMENT OF  
DEFENSE  
~~SECRETARIES OF THE MILITARY DEPARTMENTS~~

■ ■ ■

PRESIDENT, UNIFORMED SERVICES UNIVERSITY OF THE  
HEALTH SCIENCES  
DIRECTOR, CLOSE COMBAT LETHALITY TASK FORCE

SUBJECT: Comprehensive Strategy and Action Plan for Warfighter Brain Health

The Department of Defense has an enduring responsibility to promote and protect the health and well-being of the men and women of our Nation's Armed Forces. The past 17 years of conflict have taken a toll on the force in many respects. Traumatic Brain Injury (TBI) is a less visible and poorly understood consequence of this war.

TBI has been shown to result from concussive impact and exposure to blast waves. Blast exposure derives from both the effects of enemy action in combat and from training on our own weapons and tactics. Other service-related causes yet may be identified. The effects of TBI on our Service members are myriad and potentially devastating, ranging from short-term shifts in mood or the inability to sleep, to degraded cognitive performance or self-harm. Families and other Service members can struggle to understand these changes in their loved ones and teammates. Our pursuit of superior lethality must be matched by a commitment to understanding, preventing, diagnosing, and treating TBI in all its forms.

# Questions

?

# Selected Bibliography

- Bailey, Col. Pearce, M.C., et al. *The Medical Department of the United States Army in the World War. Volume X: Neuropsychiatry*. Washington: U.S. Government Printing Office, 1929.
- Bartholow, Roberts. *A Manual of Instruction for Enlisting and Discharging Soldiers*. Philadelphia, PA: J.B. Lippincott & Co., 1864.
- Boone, Katherine N. and Frank C. Richardson, "War Neurosis: A Cultural Historical and Theoretical Inquiry," *Journal of Theoretical and Philosophical Psychology* 30, no. 2 (2010): 109-121.
- Culpin, Millais, "The psychological aspect of the effort syndrome," *Lancet* 2 (1920):184-6.
- Dean, Eric T. Jr. *Shook Over Hell: Post-Traumatic Stress, Vietnam, and the Civil War*. Cambridge, MA: Harvard University Press, 1997.
- Erichsen, John E.. *On Railway and other Injuries of the Nervous System*. Philadelphia, PA: Henry C. Lea, 1867.
- Figley, Charles (ed.). *Stress Disorders Among Vietnam Veterans*. New York: Brunner/Mazel, 1978.
- Grinker, Roy R. and John P. Spiegel. *War Neuroses*. Philadelphia: Balkiston, 1945.
- Heaton, Leonard D. (ed.). *Neuropsychiatry in World War II, Volume I: Zone of the Interior*. Washington: Office of the Surgeon General, Dept. of the Army, 1966-1973.
- Goldstein, Kurt. *Aftereffects of Brain Injuries in War*. New York: Grune & Stratton, 1948.
- Gurdjian, Elisha Stephens. *Head Injury from Antiquity to the Present, with Special Reference to Penetrating Head Wounds*. Springfield, IL: Thomas, 1973.
- Hyams, Kenneth C. et al. "War Syndromes and Their Evaluation: From The U.S. Civil War to the Persian Gulf War," *Annals of Internal Medicine* 125 (1996): 398-405.
- Jones, Edgar et al. "Shell Shock: An Outcome Study of a First World War 'PIE' Unit," *Psychologica Medicine* 37 (2007): 215-233.
- Jones, Edgar et al. "Shell Shock and Mild Traumatic Brain Injury: A Historical Review," *American Journal of Psychiatry* 164, no. 11 (November , 2007): 1641-1645.
- Jones, Franklin D. et al., eds., *War Psychiatry, PI, Vol. 6, and Military Psychiatry: Preparing in Peace for War, Part I*, Vol. 7 (1995).

# Selected Bibliography

- Kardiner, Abram. *The Traumatic Neuroses of War*. New York: P. B. Hoeber, Inc., 1940.
- Kulka, R. A. et al. *Trauma and the Vietnam War Generation: Report of Findings from the National Vietnam Veterans' Readjustment Study*. Brunner/Mazel, New York, 1990.
- Macilwaine, J. E. "A Clinical study of some Functional Disorders of the Heart which occur in Soldiers," *IR Army Med Corps* 30 (1918): 357-77.
- Marlowe, David H. et al. "An Assessment of the Psychological and Psychosocial Consequences of Deployment to Desert Storm on Reserve and Active Duty Service Members in Hawaii and Pennsylvania," Annex A of *The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey*, Walter Reed Army Institute of Research, Washington, D.C., 1994.
- Marshall, Samuel Lyman Atwood. *Men Against Fire: The Problem of Battle Command in Future War*. New York: Morrow, 1947.
- Meyers, Charles Samuel. "A Contribution to the Study of Shell Shock," *Lancet* (February, 1915): 316-320.
- Mott, Frederick W. "Effects of High Explosives upon the Central Nervous System," *Lancet* (February 1916): 331-38.
- Salmon, Thomas W. "The Care and Treatment of Mental Diseases and War Neuroses ("Shell Shock") in the British Army," *Mental Hygiene* I, no. 4 (Oct., 1917): 509-47.
- Scott, Wilbur. "PTSD in DSM-III: A Case in the Politics of Diagnosis and Disease," *Social Problems* Vol. 37 (1990):294-310.
- Shephard, Ben. *A War of Nerves: Soldiers and Psychiatrists in the Twentieth Century*. Cambridge, MA: Harvard University Press, 2003.
- Talbott, John E. "Soldiers, Psychiatrists, and Combat Trauma," *Journal of Interdisciplinary History* 27, no. 3 (Winter, 1997): 437-454.
- Young, Allan. *The Harmony of Illusions: Inventing Post-Traumatic Stress Disorder*. Princeton, NJ: Princeton University Press, 1997.
- Wessely, Simon. "Twentieth-Century Theories on Combat Motivation and Breakdown," *Journal of Contemporary History* 41, no.2 (Apr., 2006): 269-86.

# WRAIR

Walter Reed Army  
Institute of Research

# 125

YEARS  
1893-2018



Soldier Health • World Health  
UNCLASSIFIED

# An Academic Perspective on the impact of WRAIR on the field of Traumatic Brain Injury

Discoveries, Innovations, Products, and the Creation of  
the Golden Age of TBI Research



SAFAR CENTER FOR  
RESUSCITATION RESEARCH  
UNIVERSITY OF PITTSBURGH



Patrick M. Kochanek, MD, MCCM

*Director, Safar Center for Resuscitation Research*

*Ake N. Grenvik Professor & Vice Chairman*

*Dept. of Critical Care Medicine*

*Professor of Anesthesiology, Pediatrics, Bioengineering, and  
Clinical & Translational Science*

*University of Pittsburgh School of Medicine*

*Editor-in-Chief, Pediatric Critical Care Medicine*

**WRAIR**

Walter Reed Army  
Institute of Research

**125**

YEARS  
1893-2018

UNCLASSIFIED



**1957-61**

**Just over 60 years ago!**



**"The grant application was only 1/2 page  
in length—that should be plenty to know  
if a project is worth funding!"**

**Peter Safar, MD**

Distinguished Professor of  
Resuscitation Medicine  
University of Pittsburgh  
School of Medicine  
**Father of Modern Day  
Resuscitation**



SAFAR CENTER FOR  
RESUSCITATION RESEARCH  
UNIVERSITY OF PITTSBURGH

**Since 1980**





**As physician scientists, it is our duty in acute medicine to define the optimal field, emergency and critical care for the injured patient!**



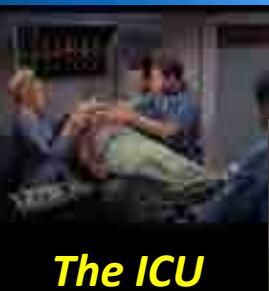
**Peter Safar loved the DoD because of its passion and genuine interest in the development of new products to improve outcomes rather than a focus on mechanisms**

# The Final Frontier in Medicine

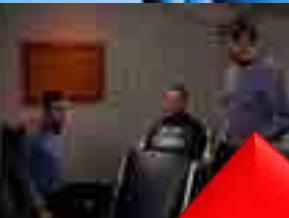
Resuscitating  
and treating  
the injured brain



*The Field*



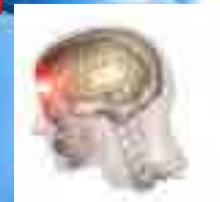
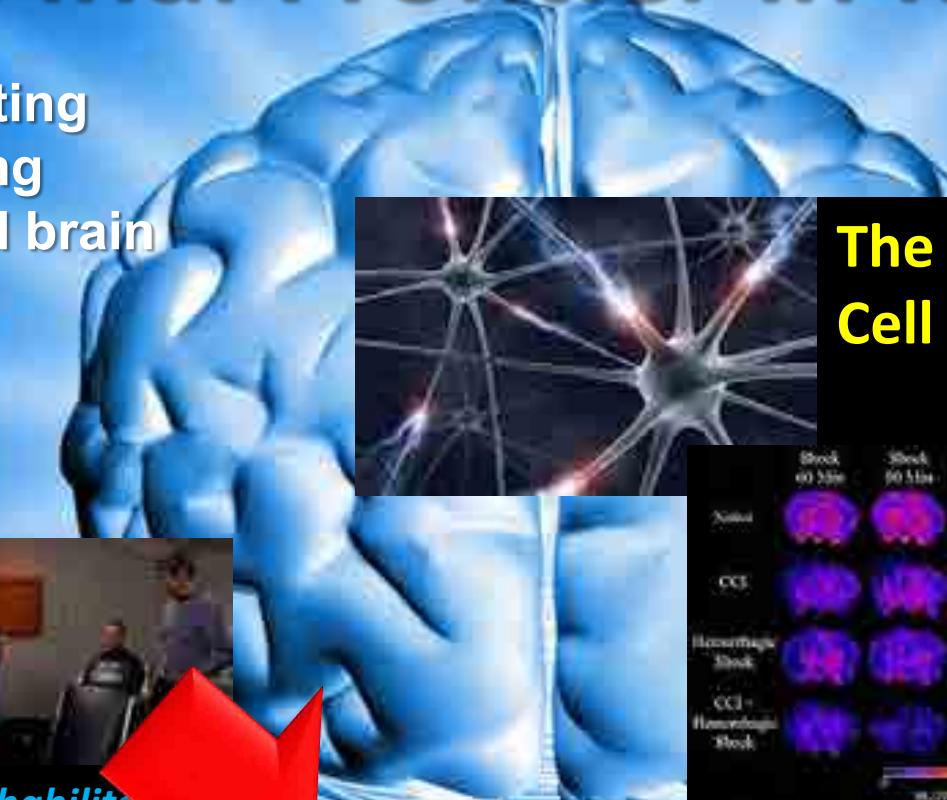
*The ICU*



*Rehabilitati*



SAFAR CENTER FOR  
RESUSCITATION RESEARCH  
UNIVERSITY OF PITTSBURGH



*Traumatic  
brain  
injury*



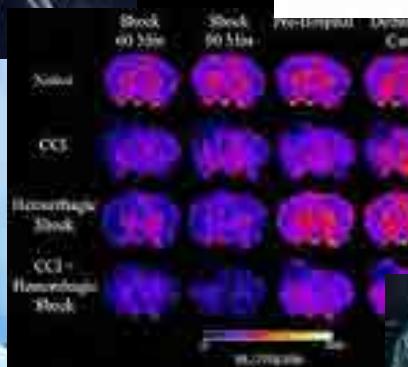
*Cardiac arrest*



*New Therapy*



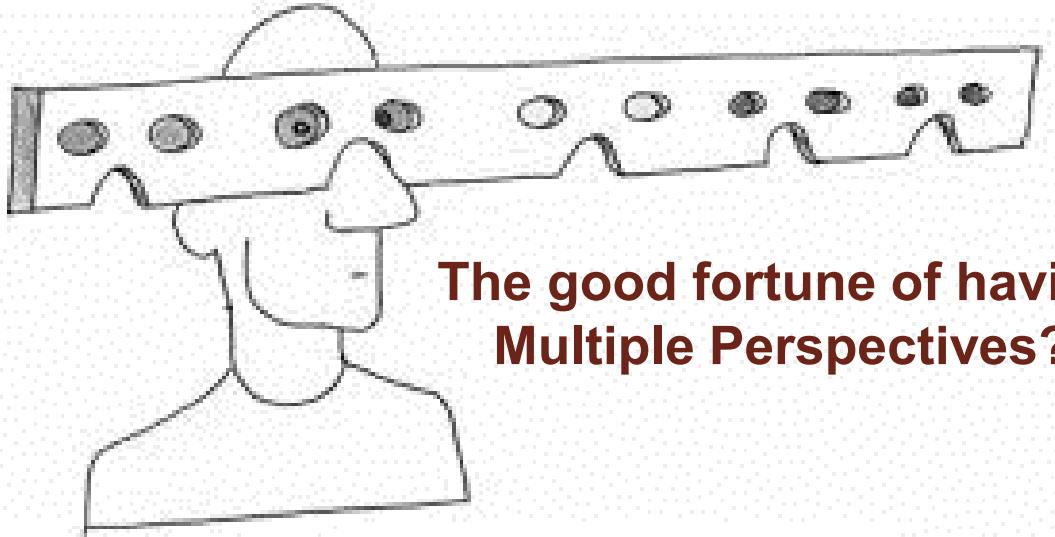
**The  
Cell**



**The realistic  
pre-clinical  
Model**



**The  
Patient**



## The good fortune of having Multiple Perspectives?



Among many others!

Many fruitful collaborations and interactions with investigators in WRAIR studying both TBI and resuscitation?

A number of DoD funded extra-mural projects in TBI?

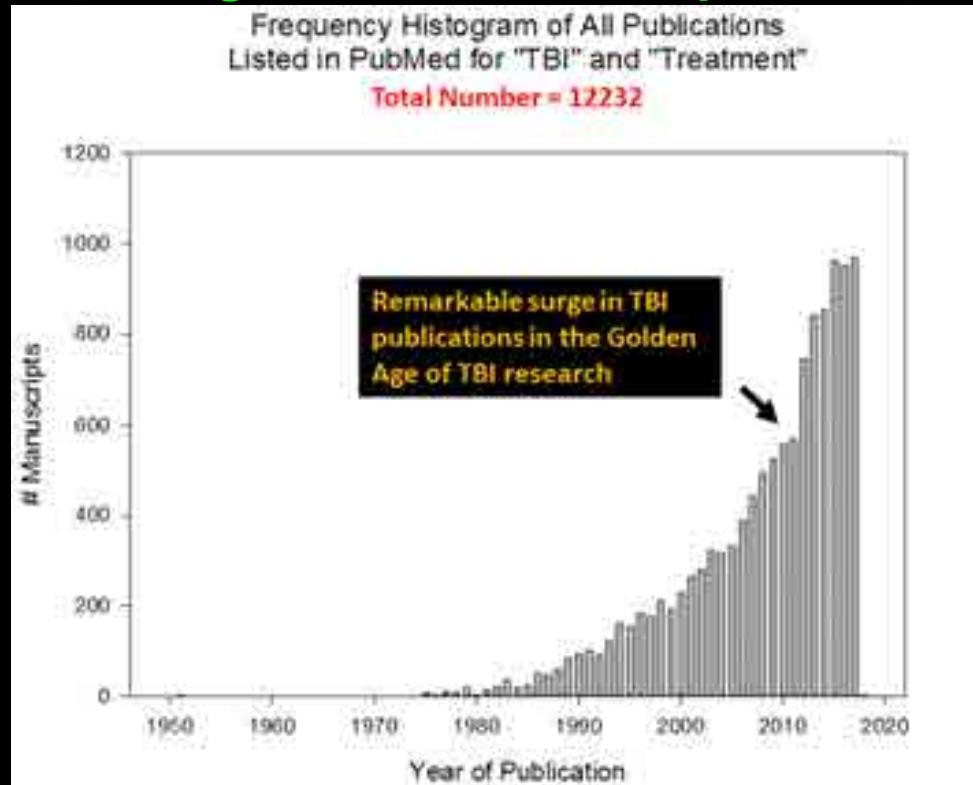
Remarkable productivity by the Safar Center in TBI?

A strong role both in civilian TBI and resuscitation research and clinical care?



The University of Pittsburgh was identified by the Institute for Scientific Information (ISI) as the top university for TBI publications in the past 15 years; and remarkably, Dr. Kochanek was identified by the ISI as the most prolific author in the field during that time period

## Recognition of the TBI epidemic



It is the  
GOLDEN  
AGE  
of TBI  
Research

Influenced greatly by the impact of the U.S. DoD on the importance of TBI, perspectives have changed!



Traumatic Brain Injury is not neuroscience—  
It's too messy!

Why did you include a clinical aim in this grant?  
Clinical TBI is too complicated to study



# Be BOLD in research!



De-risking serum biomarker development for TBI

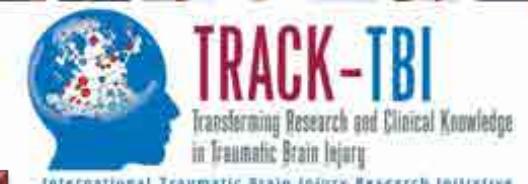
Development and testing of precision care for warfighters with TBI



Advances in Imaging



The landmark joint NCAA and DoD initiative, Concussion Assessment, Research, and Education (CARE) with 21 participating universities



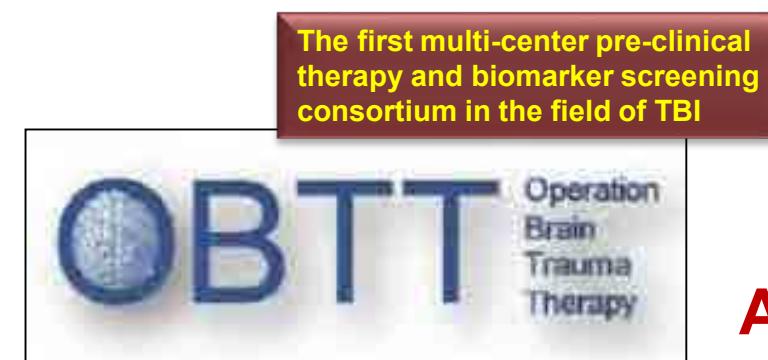
**TRACK-TBI**

Transforming Research and Clinical Knowledge  
in Traumatic Brain Injury

Biorepository and data analytics support for the NINDS-funded TRACK-TBI initiative



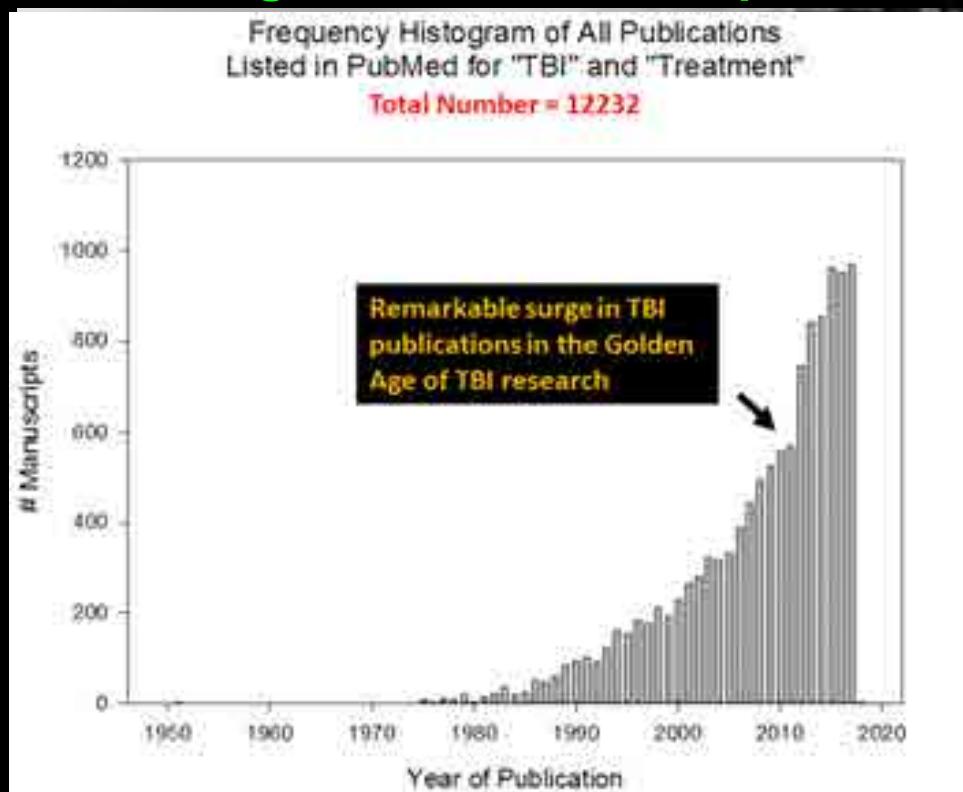
Informatics that is ready for mining and likely to pay great dividends for TBI into the future



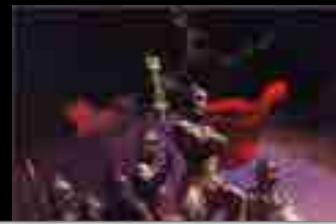
The first multi-center pre-clinical therapy and biomarker screening consortium in the field of TBI

Among many others!

# Recognition of the TBI epidemic



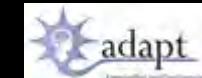
Influenced greatly by the impact of the U.S. DoD on the importance of TBI, perspectives have changed!



It is the  
**GOLDEN AGE**  
of TBI  
Research



TBI Resuscitation



**PIBIS**



**DoD funded**

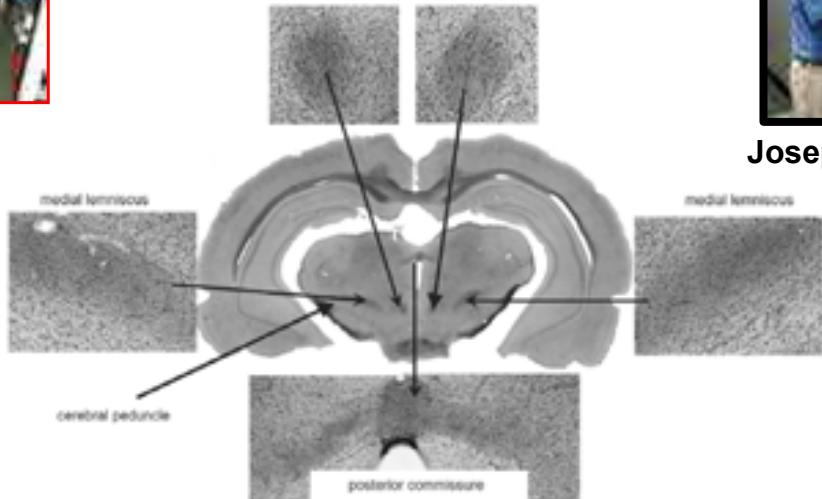
# A few examples of my own interface and collaborations with WRAIR investigators on TBI

JOURNAL OF NEUROTRAUMA 26:827-840 (June 2008)  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/neu.2008.0748



## Blast Overpressure in Rats: Recreating a Battlefield Injury in the Laboratory\*

Joseph B. Long, Timothy L. Bentley, Keith A. Wessner, Carolyn Denner, Sheena Sweeney, and Richard A. Baumgartner



Joseph Long, PhD

**"In contrast to shams, brains of rats exposed to blast showed extensive axonopathy; evident in silver-stained sections. Despite extensive fiber degeneration, the brains were devoid of any obvious cell loss"**

JOURNAL OF NEUROTRAUMA 28:1-18 (June 2011)  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/neu.2010.1944

NEU 2010-1944-2-Garman, M.  
Topic: Research Article  
**Original Article**

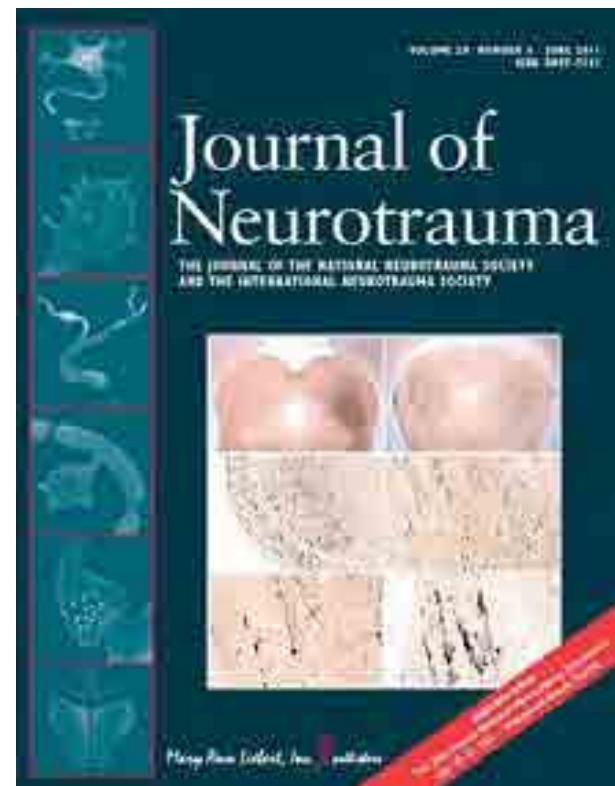


## Blast Exposure in Rats with Body Shielding is Characterized Primarily by Diffuse Axonal Injury

Robert H. Garman,<sup>1,4</sup> Larry W. Jenkins,<sup>2</sup> Robert C. Dwyer,<sup>3,6</sup> Richard A. Baumgartner,<sup>4</sup> Lawrence C. Tong,<sup>2</sup> Peter V. Shergill,<sup>7</sup> Steven A. Parks,<sup>4</sup> David V. Ritzel,<sup>8</sup> C. Edward Davis,<sup>1,4</sup> Robert S.B. Clark,<sup>3</sup> Hites Rayan,<sup>2,3</sup> Valarie Kagan,<sup>2</sup> Elizabeth K. Jackson,<sup>1,2</sup> and Patrick M. Kochanek<sup>1,4</sup>



**Robert Garman, DVM**  
In collaboration with  
Steve Parks and his  
outstanding team in the  
PREVENT program



**Cerebellar and deep white matter injury seen in multiple brain regions in rats exposed to mild blast TBI with little evidence of neuronal death**

**Garnered the cover of the *Journal of Neurotrauma* and is highly cited**



# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JUNE 2, 2011

VOL. 364 NO. 22



Christine Mac Donald, PhD



David Brody, MD, PhD

## Detection of Blast-Related Traumatic Brain Injury in U.S. Military Personnel

Christine L. Mac Donald, Ph.D., Ann M. Johnson, Dana Cooper, B.S., Elliot C. Nelson, M.D., Nicole J. Werner, Ph.D., Joshua S. Shimony, M.D., Ph.D., Abraham Z. Snyder, M.D., Ph.D., Marcus E. Raichle, M.D., John R. Witherow, M.D., \* Raymond Fang, M.D., Stephen F. Flaherty, M.D., and David L. Brody, M.D., Ph.D.

“...the scans in subjects with TBI showed marked abnormalities in the middle cerebellar peduncles...and in the right frontal white mater...”

OPEN ACCESS Freely available online

PLOS ONE

## Cerebellar White Matter Abnormalities following Primary Blast Injury in US Military Personnel

Christine Mac Donald<sup>1</sup>, Ann Johnson<sup>1</sup>, Dana Cooper<sup>1</sup>, Thomas Malone<sup>1</sup>, James Sorrell<sup>1</sup>, Joshua Shimony<sup>2</sup>, Matthew Parsons<sup>2</sup>, Abraham Snyder<sup>2</sup>, Marcus Raichle<sup>2</sup>, Raymond Fang<sup>3<sup>a</sup>b</sup>, Stephen Flaherty<sup>3<sup>a,b</sup></sup>, Michael Russell<sup>4</sup>, David L. Brody<sup>1\*</sup>

<sup>1</sup> Department of Neurology, Washington University School of Medicine, St Louis, Missouri, United States of America, <sup>2</sup> Department of Radiology, Washington University School of Medicine, St Louis, Missouri, United States of America, <sup>3</sup> Department of Trauma Surgery, Landstuhl Regional Medical Center, Landstuhl, Germany,

<sup>4</sup> Rehabilitation and Reintegration Division, US Army, San Antonio, Texas, United States of America

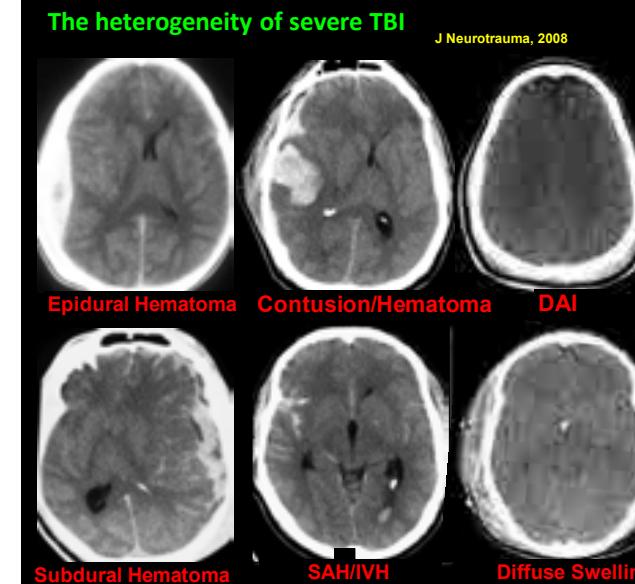
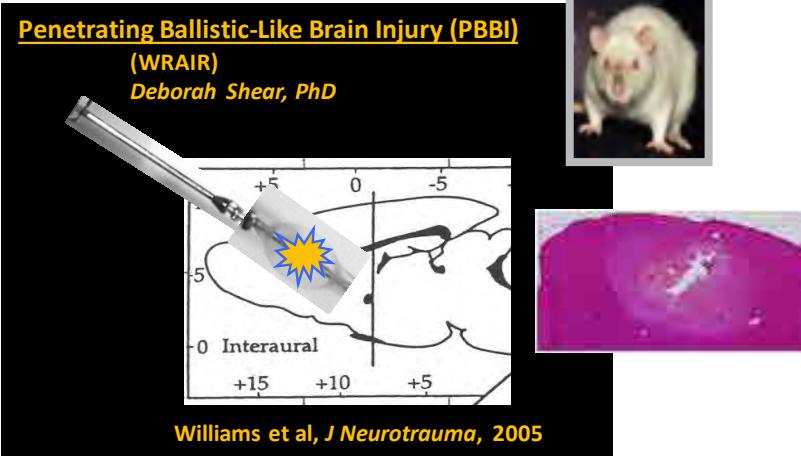


Frank Tortella, PhD

Deborah Shear, PhD

The leading investigators in the world in pre-clinical research on penetrating TBI

Over 40 publications on the penetrating ballistic-like brain injury (PBBI) model that Dr. Tortella developed



### Two hypotheses:

1. A robust therapy that crosses multiple pre-clinical models is required to translate to success in a traditional clinical RCT in severe TBI
2. Each TBI phenotype needs a different therapy?

How do we tackle the heterogeneity of TBI?

Test therapies simultaneously across multiple pre-clinical models in a highly rigorous manner; and evaluate serum biomarkers

OBTT: A powerful collaboration between leading civilian and military pre-clinical laboratories studying TBI across the USA: 3 rats models and a micro-pig model



Pre-clinical TBI rat models, sites & investigators

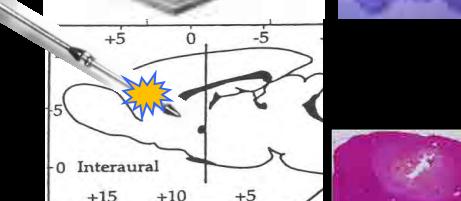
Parasagittal Fluid  
Percussion Injury (FPI)  
(University of Miami)  
W.D. Dietrich, PhD  
Helen Bramlett, PhD



Controlled Cortical Impact (CCI)  
(University of Pittsburgh)  
C. Edward Dixon, PhD



Penetrating Ballistic-Like Brain Injury (PBBI)  
(WRAIR)  
Deborah Shear, PhD  
Frank Tortella, PhD



Central FPI in micropig  
(VCU); John Povlishock, PhD, & Audrey Lafrenaye, PhD

Biomarkers (GFAP, UCH-L1)

Ron Hayes, PhD; Kevin Wang, PhD & Stefania Mondello, MD, PhD, MPH



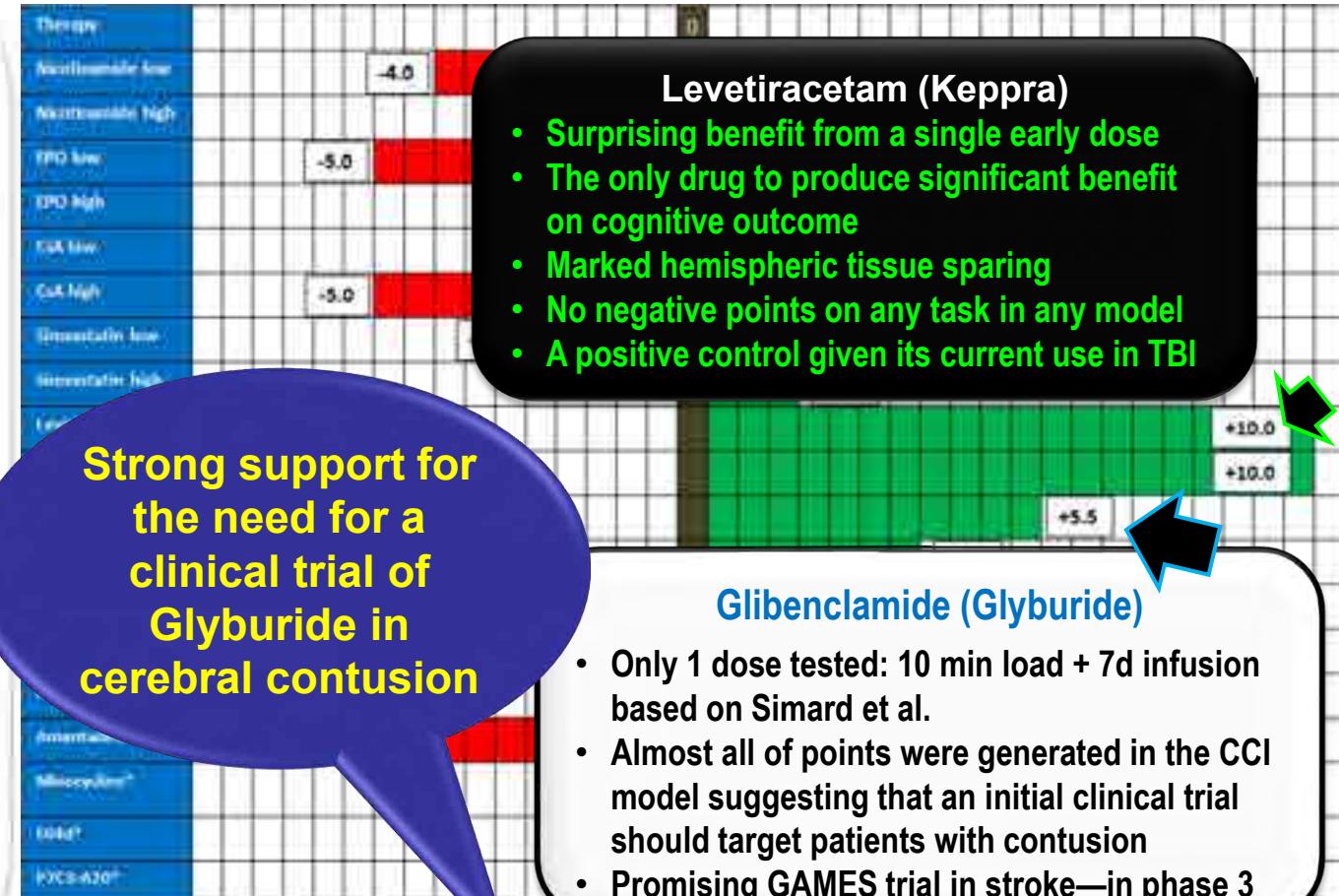
Have we found the magic bullet that crosses all the models in OBTT?

Or have we found a therapy that is highly effective in one model—  
to guide Precision Medicine?



**OBTT**  
Operation  
Brain:  
Trauma  
Therapy

Chemical structure	Dose and treatment regimen utilized	Literature support in TBI at time of selection	Therapeutic target(s)
	50 or 500 mg/kg IV 15 min and 24 h after injury	Nicotinamide 5+ studies in TBI	PARP Oxidative stress NADPH depletion  Apoptosis Inflammation Neurogenesis Angiogenesis
	5000 or 10,000 IU/kg IV at 15 min after injury	Erythropoietin 24+ studies in TBI	Mitochondrial permeability transition Ca2+-mediated Inflammation
	10 or 20 mg/kg IV 15 min and 24 h after injury	Cyclosporine A 17+ studies in TBI	HMGCo-A reductase Neuro-inflammation Cell death CBP & Trophic factors
	1 or 5 mg/kg PO—first dose 3 h after injury and then daily for 14 d	Simvastatin 14+ studies in TBI	Excitotoxicity/Seizures SV2-A/B-GABA potentiation
	64 or 110 mg/kg IV at 15 min after injury	Levetiracetam 1+ study in TBI	SUR-1 Cerebral Edema
	10 µg/kg IP 10 min post TBI then a SC infusion of 200 ng/h for 7d (Alceti)	Glibenclamide 2+ studies in TBI	Cell membrane resealing BBB
	0.2 or 0.4 g/kg IV at 15 min after injury	Kellidon VA64 1+ study in TBI	Aquaporin-4 Cerebral edema
	2.5 mg/kg IV 15 min after injury, then IV infusion 1 mg/kg/h for 48 h	AER-271 None	Dopamine augmentation Partial NMDA Antagonist
	10 or 45 mg/kg IP daily for 21 d; first dose 15 min after injury subsequent doses after testing	Amantadine 5+ studies in TBI	Neuro-inflammation Cell death
	30 mg/kg IV bolus then IV infusion of 2 mg/kg/h for 72 h	Minocycline 17+ studies in TBI	Cytokines & Calpain Inhibition
	10 mg/kg PO at 60 min after injury	E64d 1+ study in TBI	NAD salvage Neurogenesis Cell death
	10 mg/kg IP at 30 min post TBI and then RID for 7 d	P7C3-A20 4+ studies in TBI	



Strong support for  
the need for a  
clinical trial of  
Glyburide in  
cerebral contusion

### Levetiracetam (Keppra)

- Surprising benefit from a single early dose
- The only drug to produce significant benefit on cognitive outcome
- Marked hemispheric tissue sparing
- No negative points on any task in any model
- A positive control given its current use in TBI

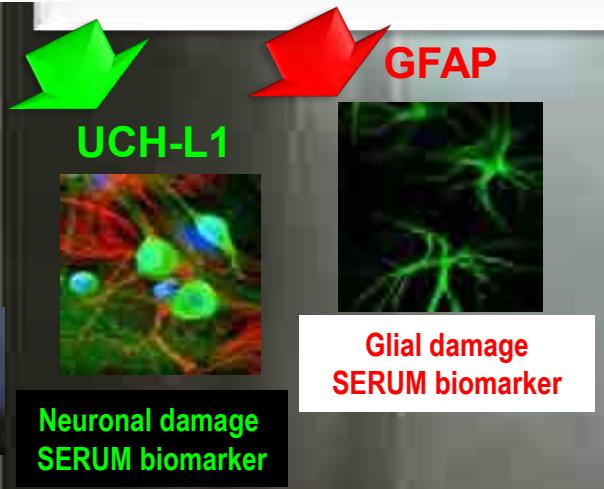
### Glibenclamide (Glyburide)

- Only 1 dose tested: 10 min load + 7d infusion based on Simard et al.
- Almost all of points were generated in the CCI model suggesting that an initial clinical trial should target patients with contusion
- Promising GAMES trial in stroke—in phase 3

Points generated by therapies tested thus far across the three models in the OBTT scoring matrix

\* = Preliminary score pending final quality control assessment and final biomarker points

## CAN WE DEVELOP A **BLOOD TEST** TO HELP DIAGNOSE, CHARACTERIZE/PHENOTYPE, AND MONITOR TBI IN OUR ANIMAL MODELS AND IN OUR PATIENTS?



In OBTT we have measured >5000 serum biomarker levels in >1500 rats  
We measured levels at 4 and 24 hours after TBI across models to assess their predictive power for both injury and for treatment effects

OBTT's mission is also to evaluate serum brain injury biomarkers across our pre-clinical models

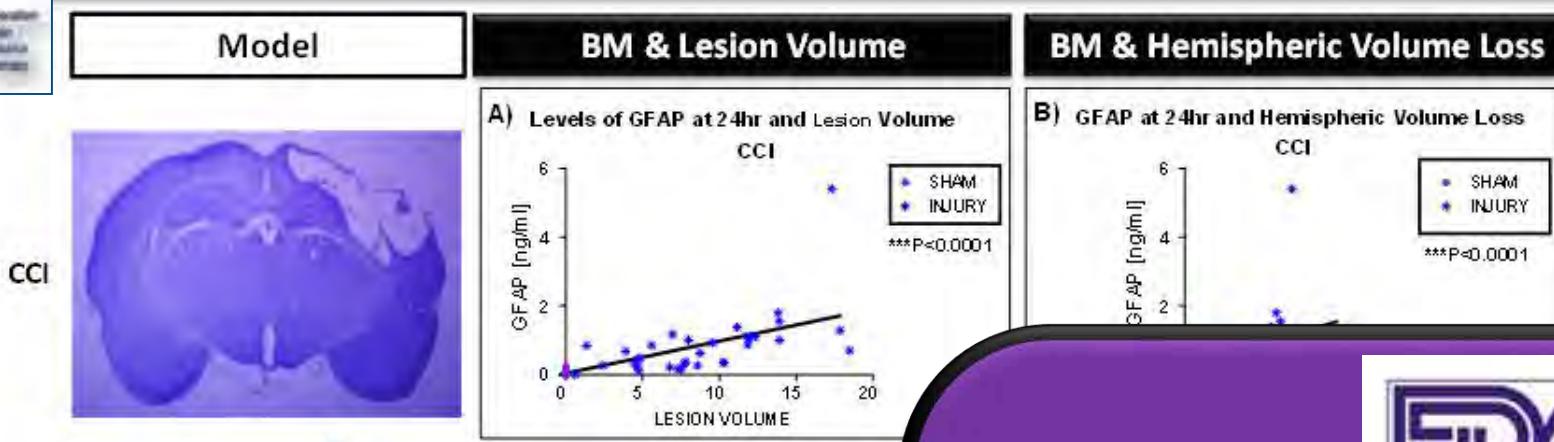
What did we find?

IT'S IN THE BLOOD

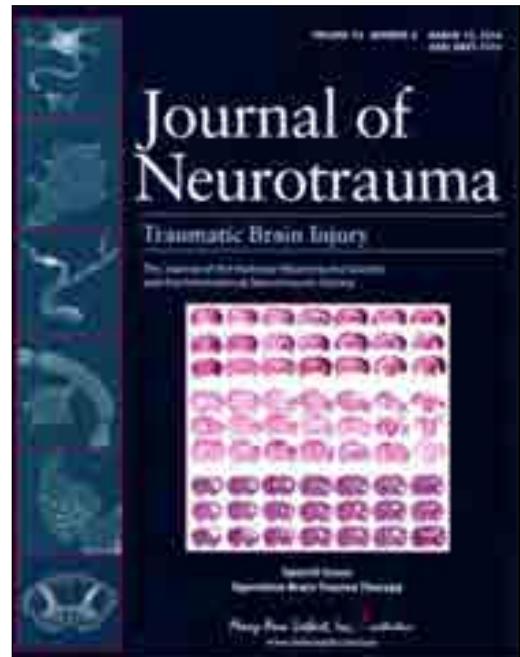
# Blood levels of GFAP at 24 h correlated with both 21 day lesion volume and hemispheric tissue loss across models: Data from the vehicle groups in the first three therapeutic trials in OBTT



WOW!



Mondello et al,  
J Neurotrauma 2016



PROMISING FINDINGS  
The 24 hour serum GFAP is a reliable biomarker of the amount of brain injury and its progression, including benefits of treatment.  
Highly predictive in animal models.



WHAT ABOUT HUMANS?

The rigorous biomarker data generated by OBTT were very favorably viewed by the FDA to compliment the clinical data in the recent successful application for approval for GFAP & UCH-L1

We are pleased that GFAP and UCH-L1 are now FDA approved for human use and that OBTT could help

I predict that they will have much more use than simply diagnosing mild TBI and will be useful in our ICUs!

UCH-L1



Neuronal damage  
SERUM biomarker

GFAP



Glial damage  
SERUM biomarker

JAMA Neurology, 2018

Original Investigation

## Time Course and Diagnostic Accuracy of Glial and Neuronal Blood Biomarkers GFAP and UCH-L1 in a Large Cohort of Trauma Patients With and Without Mild Traumatic Brain Injury

Luisa Pagan, MD, MSc; Giandomenico M. Deppeler, PhD; Robert D. Welch, MD, MSc; Lawrence M. Levine, MD; Carolina F. Braga, BA; Clara N. Tan, BS; MPH; Naema Z. Ameel, BS; Marco A. Lopez, BS; Crystal A. Hosmer, BS; Olga I. Mendez-Gordano, BS; Salvatore Silvestri, MD; Philip Giacalone, MD; Kurt D. Weber, MD; Crystal Hill-Pryor, PhD; Dallas C. Trask, MD, MPH

Editorial page 204

Supplemental content at [jamanurology.com](http://jamanurology.com)

**IMPORTANCE:** Glial fibrillary acidic protein (GFAP) and ubiquitin C-terminal hydrolase L1 (UCH-L1) have been widely studied and show promise for clinical usefulness in suspected traumatic brain injury (TBI) and concussion. Understanding their diagnostic accuracy over time will help translate them into clinical practice.

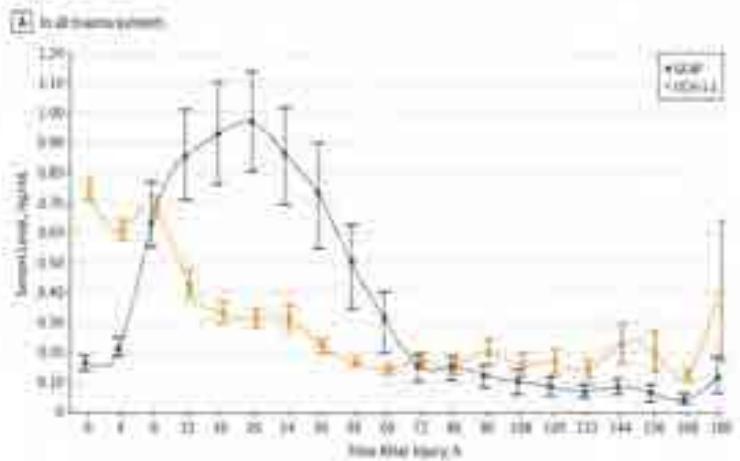
**OBJECTIVES:** To evaluate the temporal profiles of GFAP and UCH-L1 in a large cohort of trauma patients seen at the emergency department and to assess their diagnostic accuracy over time, both individually and in combination, for detecting mild to moderate TBI (MMTBI), traumatic intracranial lesions on head computed tomography (CT), and neurosurgical intervention.

**DESIGN, SETTING, AND PARTICIPANTS:** This prospective study included consecutive trauma patients seen at a level I trauma center from January 2012 to December 2013. All patients underwent neuroaxis screening to determine head trauma with loss of consciousness (Glasgow Coma Scale score of 9–15), of 30 minutes or longer, and enrollment. Of 446 patients screened, 1831 patients enrolled in the study. The mean age was 30 years (range, 16–70 years). The median time from injury to enrollment was 16 hours (range, 2–48 hours).

**MAIN OUTCOMES AND MEASURES:** The primary outcome was the presence of traumatic intracranial lesions on head CT scan.

**RESULTS:** A total of 1831 blood samples were collected from 1831 patients (mean age, 30 years; 62.0% [362 of 584] male) within 1 hour of injury. GFAP peaked at 20 hours after injury and declined to baseline by 48 hours. UCH-L1 rose rapidly and peaked at 8 hours after injury and declined to baseline by 48 hours. Over the course of 1 week, GFAP demonstrated a diagnostic range of areas under the

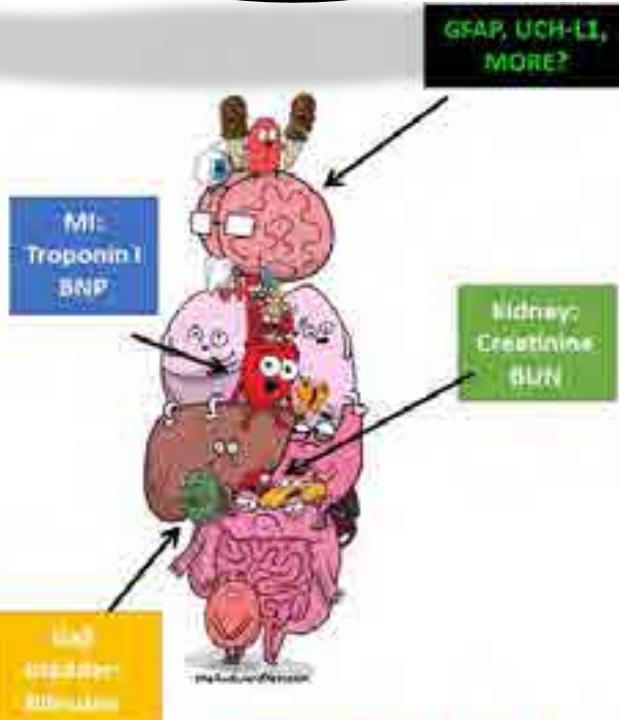
Figure 2. Temporal Profiles of Glial Fibrillary Acidic Protein (GFAP) and Ubiquitin C-terminal Hydrolase L1 (UCH-L1)



## Conclusions

In a cohort of trauma patients in whom most had mild TBI, GFAP and UCH-L1 exhibited distinct temporal profiles over the course of 7 days. Individually, GFAP outperformed UCH-L1 at all time points in diagnostic accuracy for detecting TBI, CT lesions, and neurosurgical intervention. The combination of GFAP and UCH-L1 improved GFAP diagnostic performance. These findings support the use of GFAP and UCH-L1 as biomarkers for TBI.

How about an example of where this might this be going with GFAP and UCH-L1?



# New Research at UPMC Children's Hospital of Pittsburgh using serum biomarkers:

To monitor children with cardiac arrest

To identify infant victims of abusive head trauma, and

Morbidity in children across the entire ICU

The ultimate impact of the Golden Age of  
TBI research, awakened by the DoD is  
likely to be enormous including its impact  
in the civilian arena

These are just 3  
examples

Promising findings in  
collaboration in Banyan  
Biomarkers in cardiac  
arrest

GFAP & UCH-L1  
predict outcome  
at 48 hours after  
cardiac arrest in  
children



Rachel  
Berger,  
MD, MPH

Groundbreaking studies  
using a panel of serum  
biomarkers to identify  
intracranial injury in  
infants presenting with  
silent brain injury from  
child abuse (the shaken  
baby syndrome)

Avoid missing the  
diagnosis of child  
abuse in infants at  
high risk for  
repeated injury



Ericka  
Fink MD, MS



Brain-Specific Serum Biomarkers Predict Neurological Morbidity  
in Diagnostically Diverse Pediatric Intensive Care Unit Patients

Alicia E. Au<sup>1,2</sup> · Michael J. Bell<sup>1,2</sup> · Ericka L. Fink<sup>1,2</sup> · Rajesh K. Aneja<sup>1,2</sup>  
Patrick M. Kochanek<sup>1,2</sup> · Robert S.B. Clark<sup>1,2</sup>



Alicia  
Au, MD

Use of serum biomarkers to identify  
unexpected neurological morbidity in  
103 diagnostically diverse critically ill  
children

A critically ill child  
with septic shock at  
risk for silent  
ischemic brain  
injury

A critically ill child  
with severe ARDS at  
risk for silent  
hypoxic brain injury

A critically ill  
infant with a  
silent stroke on  
ECMO



Incredible dividends have already emerged during the golden age of TBI research:

## COLLABORATION



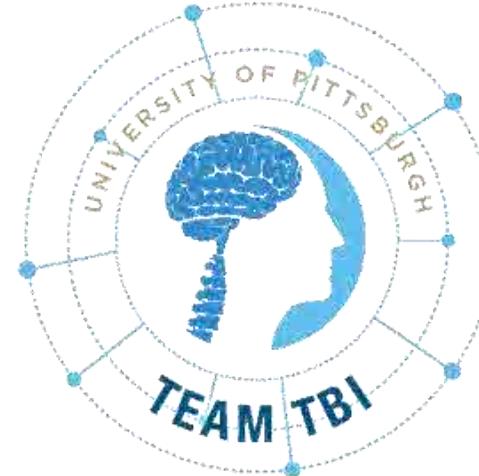
# TRACK-TBI

Transforming Research and Clinical Knowledge  
in Traumatic Brain Injury

INTERNATIONAL TRAUMATIC BRAIN INJURY RESEARCH INITIATIVE

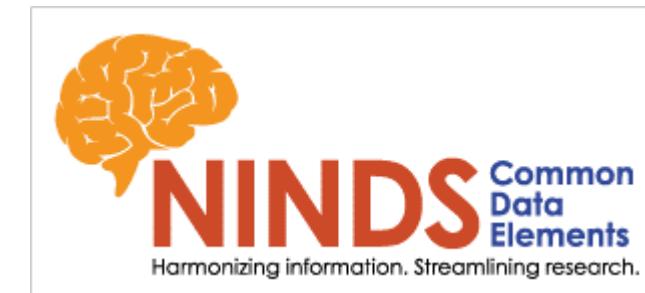


Approaches and Decisions in  
Acute Pediatric TBI Trial



# CENTER-TBI

Collaborative European NeuroTrauma Effectiveness Research in TBI  
A 2020 vision: Generating knowledge to improve TBI outcomes



# NINDS

Common  
Data  
Elements

Harmonizing information. Streamlining research.



Incredible dividends have emerged during the golden age of TBI research:

## MANAGEMENT



INTERASSOCIATION CONSENSUS:  
DIAGNOSIS AND MANAGEMENT  
OF SPORT-RELATED CONCUSSION  
BEST PRACTICES



Announcing the publication of the  
**4th Edition of the  
Guidelines for the Management of  
Severe Traumatic Brain Injury**



Learn more at [braintrauma.org](http://braintrauma.org)

**Brain Trauma**





USE OF MAGNETIC  
RESONANCE IMAGING (MRI)  
IN MANAGEMENT OF MILD  
TRAUMATIC BRAIN INJURY  
(mTBI) / CONCUSSION IN  
THE DEPLOYED SETTING

Clinical Practice Guideline





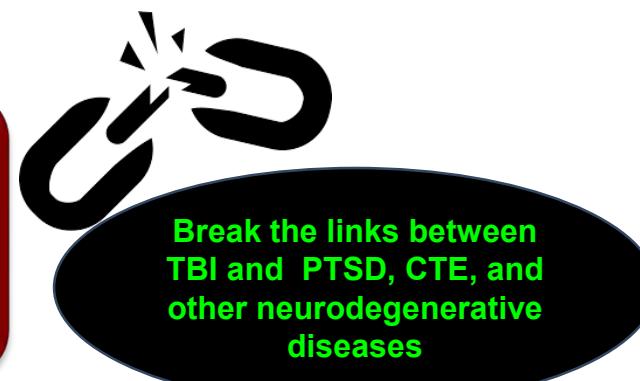
## Where is the golden age of TBI leading us?

Novel diagnostics



Novel therapies

Novel rehabilitation and outcome assessment



From Bench to Bedside

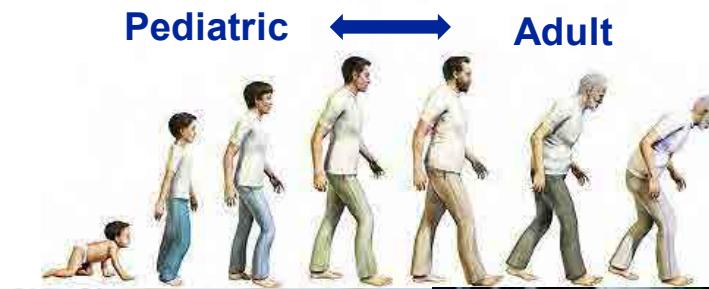
Across the spectrum of injury severity

From pediatric to geriatric

In theater or in the civilian setting



DOLMAN LAW GROUP



# PURPOSE



Research planning meeting for US Army conference on Combat Casualty Research  
2002

**It is our duty “to save  
hearts and brains  
too good to die”**



**A thousand thanks to WRAIR and the US Army  
for 125 years of vital work toward that goal**

**And in TBI and resuscitation medicine,  
we look forward to many future successful  
collaborations with WRAIR, as Government,  
Academe, and Industry link even more closely in  
the exciting new era of the DHA**



Protecting Our Nation's Top Weapon System  
The U.S. Soldier Since 1893

Protecting the most important six inches  
on the battlefield - your brain

CENTER FOR MILITARY PSYCHIATRY AND NEUROSCIENCE



Blast Induced Neurotrauma  
and Neuroprotection



Sleep & Resilience



Team Performance and  
Mental Fitness



Military Psychiatry

# WRAIR PROTECTS YOUR SIX



**WRAIR**  
125  
YEARS  
1893-2018

Walter Reed Army  
Institute of Research

Protecting the most important six microns  
between you and the threat of disease

CENTER FOR INFECTIOUS DISEASE RESEARCH



Malaria Vaccines & Entomology



Viral Diseases & Bacterial  
Diseases



Military HIV Research Program



Experimental Therapeutics &  
Emerging Infectious Disease

WHETHER YOU'RE AT HOME STATION OR SIX THOUSAND MILES AWAY

Soldier Health • World Health

# WRAIR

Walter Reed Army  
Institute of Research

# 125

YEARS  
1893-2018



Soldier Health • World Health  
UNCLASSIFIED

# **Transformation of Behavioral Health (BH) Care Since 9/11: Impact of WRAIR Research**

**Charles W. Hoge, M.D.  
Center for Psychiatry and Neuroscience,  
Walter Reed Army Institute of Research  
and  
Office of the Army Surgeon General (OTSG)**

**(This brief reflects the personal opinions of the author, not  
official position of WRAIR, Army, or DoD.)**



**125**  
YEARS  
1893-2018



# Deployment Mental Health Screening: Background

- Gulf War I (1990-91) veterans experienced multiple mental health concerns that were not addressed for years
- 1998 (Kosovo). DoD screening first mandated, but only a single question
- However, from 1996-2000, WRAIR/USAMRU-E researchers fielded other screening prototypes in Soldiers deployed to Bosnia and Kosovo.



PLEASE FILL IN SOCIAL SECURITY #

			-			-				
--	--	--	---	--	--	---	--	--	--	--

## Health Assessment

1. Would you say your health in general is:  
 Excellent    Very Good    Good    Fair    Poor
2. Do you have any unresolved medical or dental problems that developed during this deployment?  
 Yes    No
3. Are you currently on a profile or light duty?  
 Yes    No
4. During this deployment have you sought, or intend to seek, counseling or care for your mental health?  
 Yes    No
5. Do you have concerns about possible exposures or events during this deployment that you feel may affect your health?  
 Yes    No

# 2001-2003: Salient Events

- 9/11, start of OEF, cluster of murder-suicides at Ft. Bragg (2002), start of OIF (2003)
- DoD initiated Post-Deployment Health Assessment (PDHA)
- WRAIR launched large research initiative (*real-time, occupationally-relevant*):
  - Land Combat Study
  - Mental Health Advisory Team (MHAT) Assessments in Iraq and Afghanistan
  - Research focus especially on screening, education, and health care services



# **Combat Experiences, U.S. Infantry**

## **Land Combat Study (n=18,305)**

Receiving incoming artillery, rocket, mortar



Being attacked or ambushed



Knowing someone seriously injured or killed



Seeing injured women / children you  
were unable to help



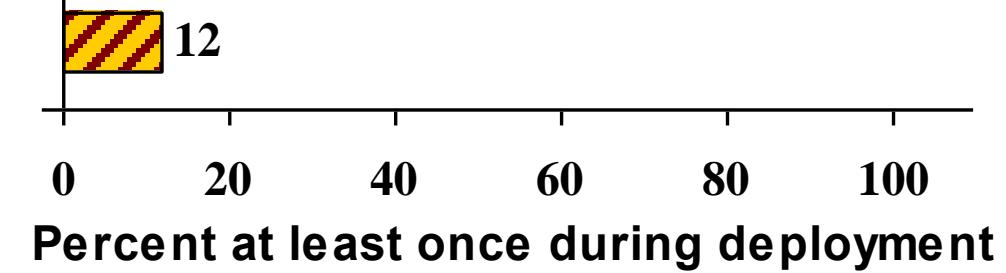
Responsible for death of enemy combatant



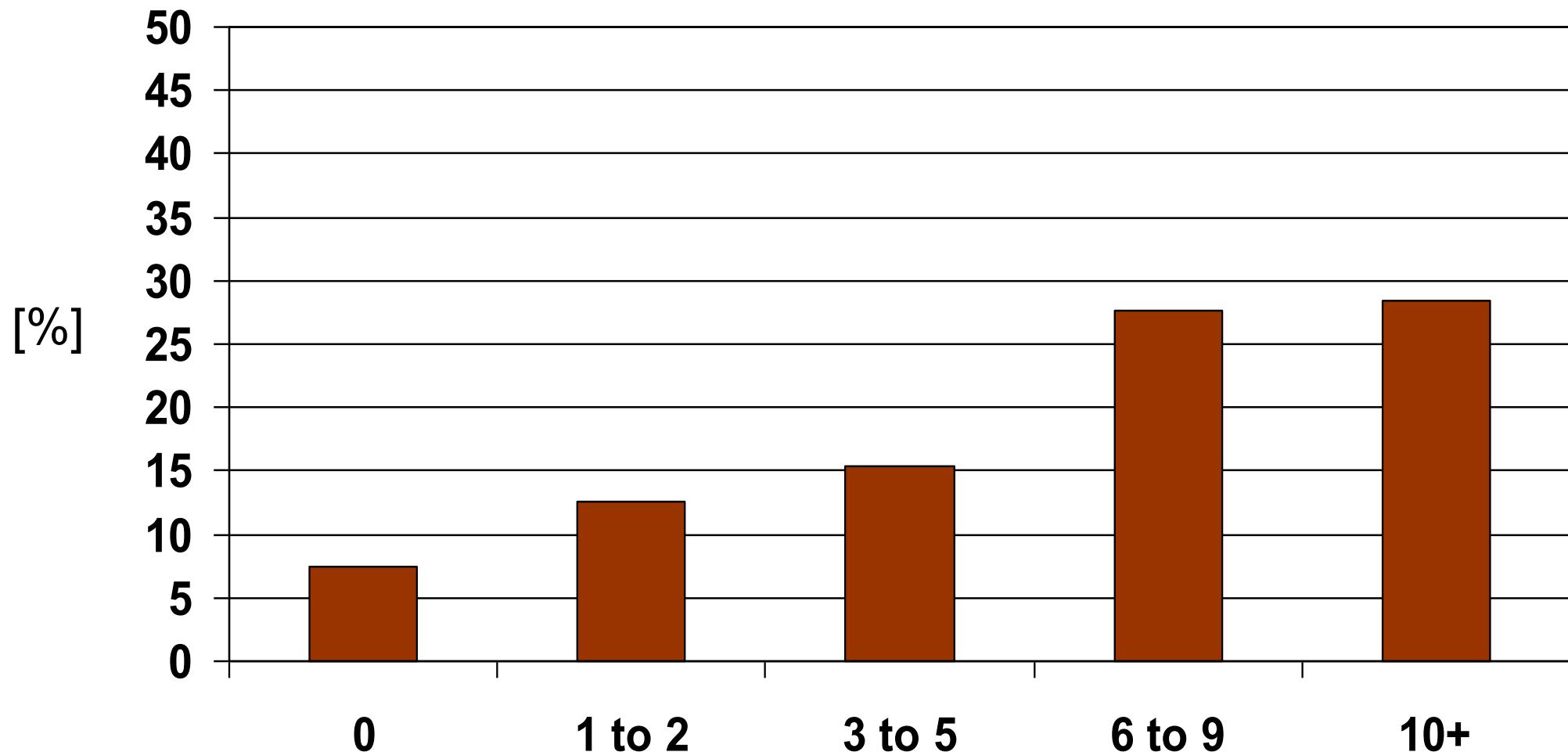
Being wounded or injured



Shot or hit but protective gear saved you



# **PTSD Prevalence by Number of Firefights During Deployment, Iraq / Afghanistan**



• WRAIR Land Combat Study, 3-4 months post-deployment

2004

**NOTICE**

GOES ON  
PERMANENT  
RECORD

YOU MIGHT LOSE  
YOUR SECURITY  
CLEARANCE

**DANGER**

SEEING A "SHRINK"  
IS HAZARDOUS  
TO YOUR CAREER

**CAUTION**

SEEKING HELP IS  
A SIGN OF  
WEAKNESS

*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

JULY 1, 2004

VOL. 351 NO. 1



Combat Duty in Iraq and Afghanistan,  
Mental Health Problems, and Barriers to Care

Charles W. Hoge, M.D., Carl A. Castro, Ph.D., Stephen C. Messer, Ph.D., Dennis McGurk, Ph.D.,  
Dave I. Cotting, Ph.D., and Robert L. Koffman, M.D., M.P.H.

# Perceived Stigma of Mental Health Care

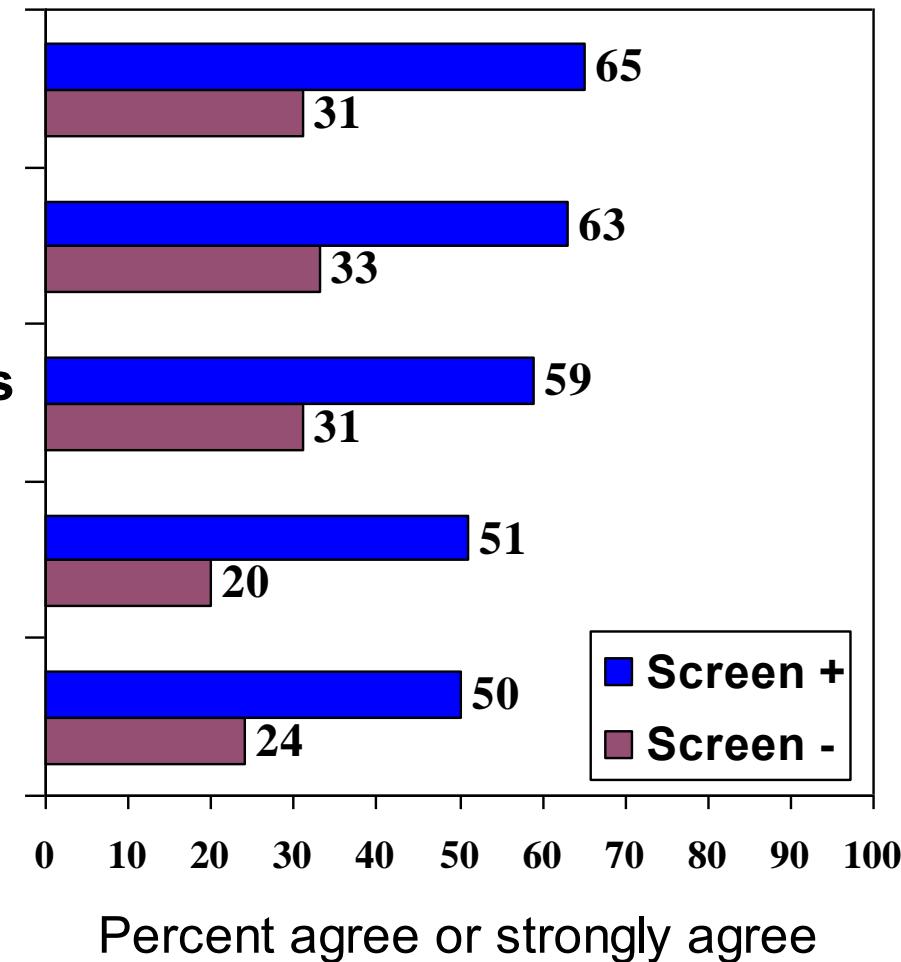
**I would be seen as weak.**

**My unit leadership might treat me differently.**

**Members of my unit might have less confidence in me.**

**My leaders would blame me for the problem.**

**It would harm my career.**



\*Participants were asked to “rate each of the possible concerns that might affect your decision to receive mental health counseling or services if you ever had a problem”

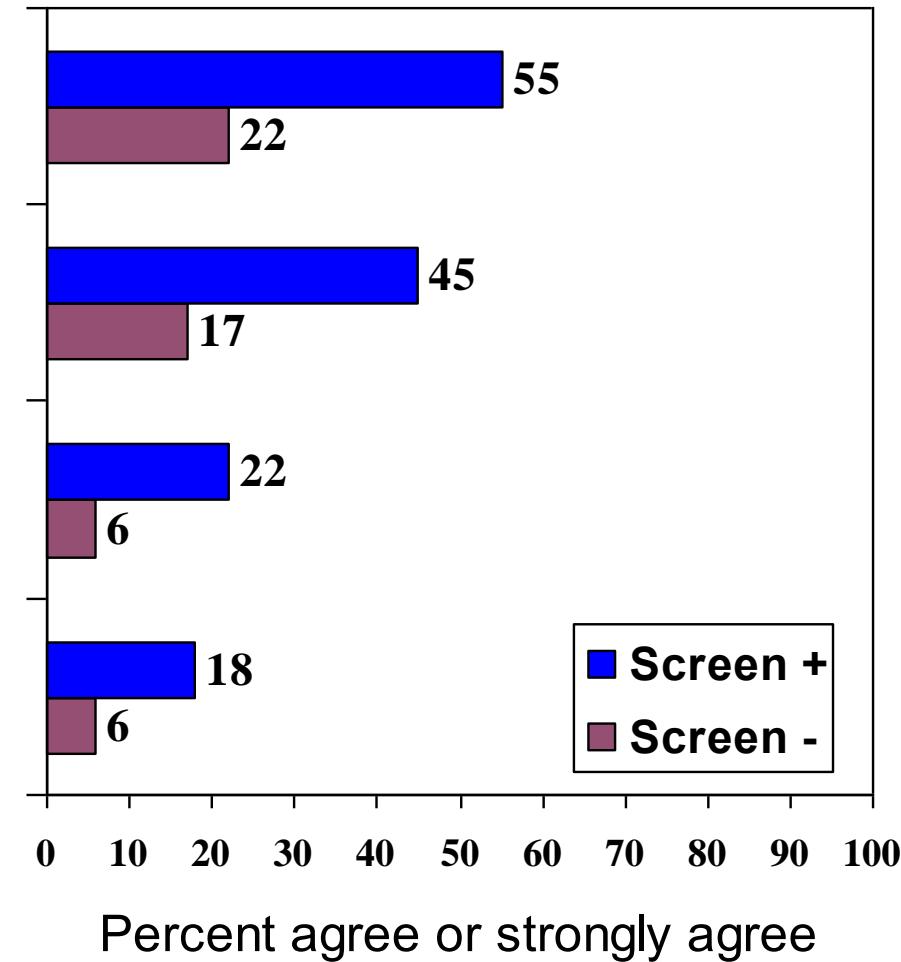
# Other Perceived Barriers to Mental Health Care

**There would be difficulty getting time off work for treatment.**

**It is difficult to schedule an appointment.**

**I don't know where to get help.**

**I don't have adequate transportation.**



# 2004-2006: Key WRAIR Research Findings

- Poor structure and distribution of BH care in theater to support shift from divisions to BCTs (MHATs) (prevention & treatment teams)
- Major gap in timing of post-deployment health (PDHA) screening



US Army Medical Research Unit - Europe  
Walter Reed Army Institute of Research  
LTC Paul Bliese (paul.bliese@us.army.mil)  
Dr. Kathleen Wright (kathleen.wright@us.army.mil)  
Dr. Amy Adler (amy.adler@us.army.mil)  
CPT Jeffrey Thomas (jeffrey.l.thomas@us.army.mil)

Psychological Services  
2007, Vol. 4, No. 3, 141-148

Copyright 2007 by the American Psychological Association  
1541-1559/07/\$12.00 DOI: 10.1037/1541-1559.4.3.141

(197)  
Timing of Postcombat Mental Health Assessments

Paul D. Bliese, Kathleen M. Wright, Amy B. Adler, Jeffrey L. Thomas, and  
Charles W. Hoge  
Walter Reed Army Institute of Research

# 2005-2006 – Army/DoD Response to Research Findings

FM 4-02.51 (FM 8-51)

- Post-Deployment Screening
  - PDHRA added (90-120 days).
- Training and BH Health Care:

Major restructuring of care:

  - Large increased in BH personnel directly supporting BCTs
  - COSC doctrine and training extensively revised
  - Small BH mobile teams trained to provide full range of services

---

**COMBAT AND OPERATIONAL  
STRESS CONTROL**

---

JULY 2006

DISTRIBUTION RESTRICTION: Approved for public release; distribution is unlimited.

---

Headquarters, Department of the Army

---

# 2007: Problems with Care at Walter Reed



# 2007 Response to Walter Reed Scandal

- WRAIR benchmark data (including Congressional testimonies) strongly influenced task force findings

- DoD Mental Health Task Force
- Independent Review Group
- President's Commission



- Conclusions: DoD programs insufficient to meet mental health needs of service members
  - 300+ recommendations
  - \$900M initial Congressional appropriation for PTSD/TBI research and treatment
  - WRAIR research guided prioritization of efforts

ARMY ANNOUNCES RESULTS OF MENTAL HEALTH ADVISORY TEAM SURVEY  
U.S. Army News : Public Affairs | March 25, 2004 | U.S. Army  
Printed 2/24/04 8:42:18 PM by [mashall](#)

Operation Iraqi Freedom (OIF)  
Mental Health Advisory Team (MHAT)

REPORT

15 December 2003

Chartered by:  
U.S. Army Surgeon General  
& HQDA G-1

Operation Iraqi Freedom (OIF-II)

Mental Health Advisory Team (MHAT-II)

REPORT

30 January 2005

Chartered by:  
The U.S. Army Surgeon General

JAMA Psychiatry

ORIGINAL CONTRIBUTION

(2002)

Mental Health Problems, Use of  
Mental Health Services, and Attrition  
From Military Service After Returning  
From Deployment to Iraq or Afghanistan

Charles W. Hoge, M.D.  
Jennifer L. Auchterback, M.S.  
Charles A. Milliken, M.D.

The NEW ENGLAND (4959)  
JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 1, 2004

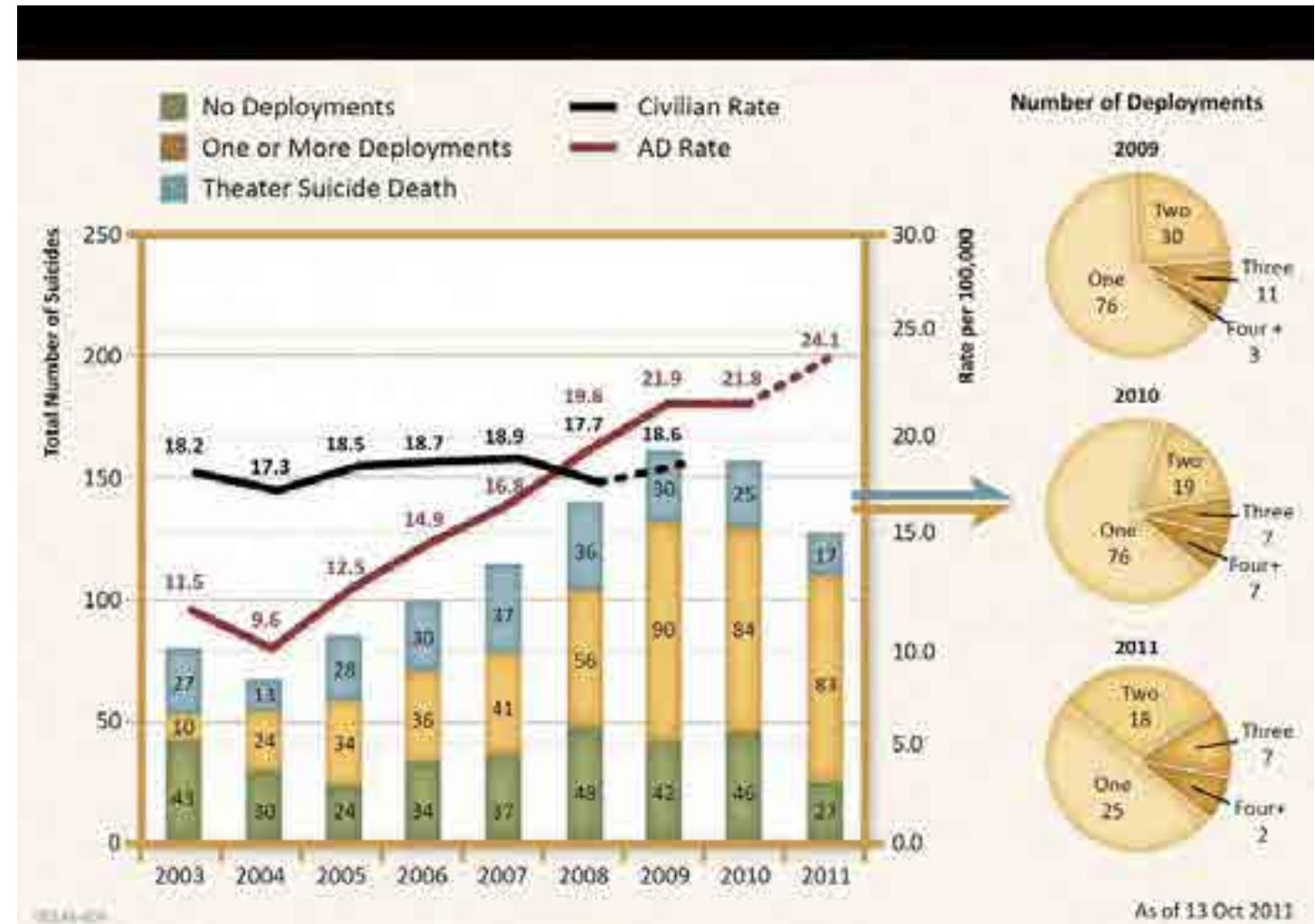
VOL. 351 NO. 1

Combat Duty in Iraq and Afghanistan,  
Mental Health Problems, and Barriers to Care

Charles W. Hoge, M.D., Carl A. Castro, Ph.D., Stephen C. Messer, Ph.D., Dennis McGurk, Ph.D.,  
Dave I. Cotting, Ph.D., and Robert L. Koffman, M.D., M.P.H.

# 2008: Evolving Problems

- ▶ However, BH problems persisted and worsened.
- ▶ TBI also emerged as “signature injury” of OIF/OEF.
- ▶ Army / DoD began transforming BH care.



# 2008-2018—WRAIR Research Impact on Transformation of BH Care: Screening

- ▶ Validation of DoD PTSD screening tool
- ▶ Refined DoD screening (2-stage process)
- ▶ Screening combined with care coordination

Journal of Trauma and Acute Physiology  
2008; Vol 65, No 2, pp 222-227

**(626)**  
Validating the Primary Care Posttraumatic Stress Disorder Screen and the Posttraumatic Stress Disorder Checklist With Soldiers Returning From Combat.

Paul D. Bliese, Kathleen M. Wright, Amy B. Adler,  
and Oscar Cabezas  
U.S. Army Medical Research Unit—Europe

Carl A. Castro and Charles W. Hoge  
Walter Reed Army Institute of Research

**Article**  
**Effectiveness of Mental Health Screening and Coordination of In-Theater Care Prior to Deployment to Iraq: A Cohort Study (81)**

Christopher R. Warner, M.D.

George N. Appenzeller, M.D.

Jessica R. Parker, Psy.D.

Carolynn M. Warner, M.D.

Charles W. Hoge, M.D.

**Objective:** The authors assessed the effectiveness of a innovative method of pre-deployment mental health screening to determine whether screening decreased negative outcomes during deployment in Iraq's combat setting.

**Method:** Primary care providers performed directed mental health screening during standard predeployment medical screening. If indicated, onsite mental

with additional requirements. After 6 months, soldiers in screened brigades had significantly lower rates of clinical contacts after the battle, ie, increased brigades for medical liaison (0.4%, 10%) (CI=0.7%–E.1), for combat stress (15.7%, 25%) (CI=13.1%–18.4), compared with 0.9%, 10% (CI=0.7%–E.1), for combat stress (15.7%, 25%) (CI=13.1%–18.4), compared with 22.0%, 10% (CI=22.2%–22.8%), and for psychiatric disorders (2.9%, 0.9% (CI=2.6%–3.2), compared with 13.2%, 0.9% (CI=12.3%–13.8), as well as

**(190)**

**Estimating Population Prevalence of Posttraumatic Stress Disorder: An Example Using the PTSD Checklist**

James T. Foa  
Center for the Study of Traumatic Stress, Uniformed Services University of the Health Sciences, Bethesda, MD

Nancy Foa  
Institute and Clinical Epidemiology Service, National Institute of Mental Health, Bethesda, MD

Charles C. Engel  
Center for the Study of Traumatic Stress, Uniformed Services University of the Health Sciences, Bethesda, MD

Paula F. Schmidt  
National Center for PTSD, VA Medical Center, White River Junction, VT

Charles W. Hoge  
University of Psychiatry and Neuroscience, Walter Reed Army Institute of Research, U.S. Army Medical

**ORIGINAL ARTICLE**

**(191)**  
Importance of Anonymity to Encourage Honest Reporting in Mental Health Screening After Combat Deployment

Christopher R. Warner, M.D.; George N. Appenzeller, M.D.; Thomas Grupper, M.D.; Karen Krebsbach, M.P.H.; Paul Fontenot; Perry J. Larson; Parker, Psy.D.; Carolyn R. Wrayne, M.D.; Charles W. Hoge, M.D.

# 2008-2018—WRAIR Research Impact on Transformation of BH Care: Diagnosis

- ▶ Changes in DSM-5 PTSD definition (A2 criterion) (2013)
- ▶ Validation of cutoff values for new DSM-5 PTSD screener
- ▶ VA/DoD Clinical Practice Guideline (CPG) screening and diagnosis sections (2017), and Army/DoD PTSD policies

THE LANCET  
Psychiatry

(174)

The prevalence of post-traumatic stress disorder (PTSD) in US combat soldiers: a head-to-head comparison of DSM-5 versus DSM-IV-TR symptom criteria with the PTSD checklist

JAMA Psychiatry

Special Communication

(45)

Unintended Consequences of Changing the Definition of Posttraumatic Stress Disorder in DSM-5  
Critique and Call for Action

Charles W. Hoge, MD; Rachel Yehuda, PhD; Carl A. Castro, PhD; Alexander C. McFarlane, MD; Eric Vermetten, MD, PhD; Rakesh Jolly, MD; Karenian C. Koemmel, PhD; Neil Greenberg, MD; Arieh Y. Shalev, MD; Sheila A. M. Rauch, PhD; Charles R. Marmar, MD; Barbara C. Rothbaum, PhD

(122)

A2 Diagnostic Criterion for Combat-Related Posttraumatic Stress Disorder

Anny B. Adler; Kathleen M. Wright; Paul D. Bliese; and Rachel Eckford  
*U.S. Army Medical Research & Materiel Command, Walter Reed Army Institute of Research, Bethesda, Maryland*  
Charles W. Hoge  
*Divisions of Psychiatry and Neuroscience, Walter Reed Army Institute of Research, Bethesda, Maryland*

# 2008-2018—WRAIR Research Impact on Transformation of BH Care: Clinical Treatment

Review **JAMA** The Journal of the American Medical Association

## Psychotherapy for Military-Related PTSD A Review of Randomized Clinical Trials

Maria M. Steenkamp, PhD; Brett T. Litz, PhD; Charles W. Hoge, MD; Charles R. Marmar, MD

EDITORIAL

(7)

## A Window Into the Evolution of Trauma-Focused Psychotherapies for Posttraumatic Stress Disorder

Charles W. Hoge, MD; Kathleen M. Chait, PhD

**JAMA Psychiatry**

(144)

## Interventions for War-Related Posttraumatic Stress Disorder

Meeting Veterans Where They Are

## Use of Evidence-Based Treatment (28) for Posttraumatic Stress Disorder in Army Behavioral Healthcare

Joshua E. Wilk, Joyce C. West, Farifteh F. Duffy, Richard K. Herrell, Donald S. Rae, and Charles W. Hoge

(237)

**JAMA Psychiatry**

(19)

## The Meaning of Evidence-Based Treatments for Veterans With Posttraumatic Stress Disorder

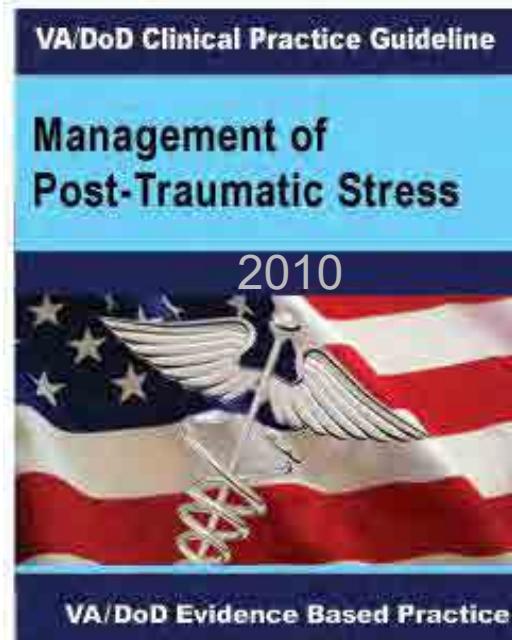
VIEWPOINT

### Research Article

(80)

#### PSYCHOTHERAPY VERSUS PHARMACOTHERAPY FOR POSTTRAUMATIC STRESS DISORDER: SYSTEMIC REVIEW AND META-ANALYSES TO DETERMINE FIRST-LINE TREATMENTS

Daniel J. Lutz, M.D.,<sup>1,2,3</sup> Carlo W. Schmitzkin, D.O.,<sup>1,2</sup> Jonathan P. Wolf, M.D.,<sup>4</sup> Misra Vythilingam, M.D.,<sup>1</sup> Ann M. Harrison, M.D.,<sup>1,2,3</sup> and Charles W. Hoge, M.D.<sup>2</sup>



## VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF POSTTRAUMATIC STRESS DISORDER AND ACUTE STRESS DISORDER

2017

Department of Veterans Affairs

Department of Defense

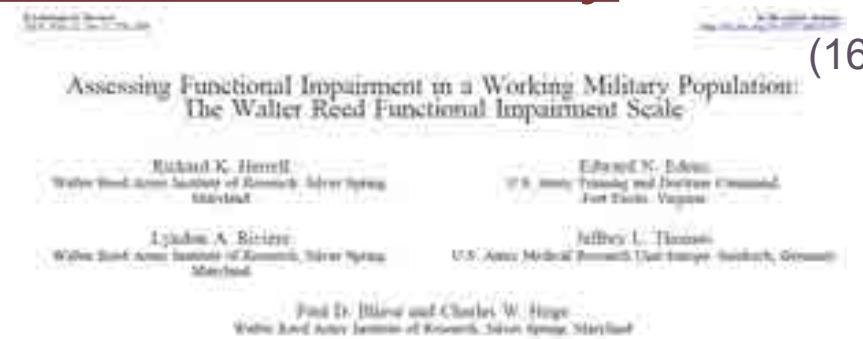
# 2008-2018—WRAIR Research Impact on Transformation of BH Care: Clinical Care Delivery

- ▶ Behavioral Health Data Portal (BHDP):
  - ▶ WRAIR Functional Impairment Scale
  - ▶ Therapeutic alliance measures
- ▶ Stigma/barriers and leadership research informed structure of BH care:
  - ▶ Embedded Behavioral Health (EBH)
  - ▶ BH in primary care

BJPsych

## Longitudinal determinants of mental health treatment-seeking by US soldiers (34)

Amy B. Adler, Thomas W. Britt, Lyndon A. Riviere, Paul Y. Kim and Jeffrey L. Thomas



## PTSD Treatment for Soldiers After Combat Deployment: Low Utilization of Mental Health Care and Reasons for Dropout (160)

Charles W. Hoge, M.D.,  
Sasha H. Grossman, B.A.,  
Jennifer L. Ambrosini, M.S.,  
Lyndon A. Riviere, Ph.D.,  
Charles S. Milliken, M.D.,  
Joshua E. Wilk, Ph.D.

Published online March 2014

(28)

## Stigma, Negative Attitudes About Treatment, and Utilization of Mental Health Care Among Soldiers (257)

Paul Y. Kim  
Walter Reed Army Institute of Research, Silver Spring, Maryland

Thomas W. Britt  
Clemson University, Clemson, South Carolina

Robert P. Klocko and Lyndon A. Riviere  
Walter Reed Army Institute of Research, Silver Spring, Maryland

Amy B. Adler  
U.S. Army Medical Research Unit-Europe, Walter Reed Army Institute of Research, Heidelberg, Germany

## Use of Evidence-Based Treatment for Posttraumatic Stress Disorder in Army Behavioral Healthcare

Joshua E. Wilk, Joyce C. Breaux, Farzad I. Doshi, Richard K. Herrell, Donald S. Mat, and Charles W. Hoge

# 2008-2018—WRAIR Research Impact on Transformation of BH Care: Benchmarking

## ORIGINAL ARTICLE

The Journal of Nervous and Mental Disease

(163)

### Posttraumatic Stress Disorder Associated With Combat Service in Iraq or Afghanistan

Reconciling Prevalence Differences Between Studies

Brian C. Kok, BA; Richard K. Herrell, PhD; Jeffrey L. Thomas, PhD; and Charles W. Hoge, MD

(32)

### Transformation of Mental Health Care for U.S. Soldiers and Families During the Iraq and Afghanistan Wars: Where Science and Politics Intersect

Charles W. Hoge, MD; Christopher G. Griswold, MD; Edward A. Busnel, MA, LW; Michael D. Bostick, MD; John C. Sheng, MPH; Amy B. Atiles, PhD; Christopher H. Warner, MHS; David T. Chiravasi, MD

MILITARY MEDICINE, 173, 11:101, 2008

(243)

### Prevalence of Mental Health Problems, Treatment Need, and Barriers to Care among Primary Care-Seeking Spouses of Military Service Members Involved in Iraq and Afghanistan Deployments

Karen M. Eaton, MS<sup>1</sup>; COL Charles W. Hoge, MC USA<sup>2</sup>; Stephen C. Messer, PhD<sup>1</sup>; Allison A. Whitt, BS<sup>1</sup>; CPT Oscar A. Cabrera, MS USA<sup>2</sup>; MAJ Dennis McGurk, MS USA<sup>2</sup>; LTC Anthony Cox, MS USA<sup>2</sup>; COL Carl A. Castro, MS USA<sup>2</sup>

(41)

### 2003-2009 Marital Functioning Trends Among U.S. Enlisted Soldiers Following Combat Deployments

James A. Wilson, PhD; COL Jeffrey L. Thomas, MAC USA<sup>1</sup>; Joshua E. Will, PhD; LTC Jeffery L. Thomas, MAC USA<sup>1</sup>; Brian C. Hoge, PhD; LTC Carl A. Castro, MAC USA<sup>1</sup>

## JAMA Psychiatry

(1736)

### Longitudinal Assessment of Mental Health Problems Among Active and Reserve Component Soldiers Returning From the Iraq War

Charles S. Minkler, MD  
Jennifer L. Auerbach, MS  
Charles W. Hoge, MD

(50)

### Trends in Mental Health Services Utilization and Stigma in US Soldiers From 2002 to 2011

Joseph J. Gonnella, PhD; Andrew F. Monk, PhD; Jennifer L. Thomas, PhD; Robert R. Rugg, PhD; Andrew J. P. Herrell, PhD; John M. Stroh, PhD; Brian C. Hoge, PhD; Richard V. Klim, MA; Anthony Chiravasi, MA; and Charles W. Hoge, PhD

## JAMA

(99)

### Preventing Suicides in US Service Members and Veterans: Concerns After a Decade of War

Charles W. Hoge, MD  
Carl A. Castro, PhD

## JAMA Internal Medicine

(66)

### Chronic Pain and Opioid Use in US Soldiers After Combat Deployment

Jeffrey L. Thomas, PhD, MPH  
Philip C. Griswold, PhD  
Jordan A. Knutson, PhD  
Katherine Clark-Watson, MPH  
Charles W. Hoge, MD

## BJPsych

(90)

### Mental health outcomes in US and UK military personnel returning from Iraq

Mark J. Lewis, Louise A. Vasey, Linda A. Ross, Helen J. Macdonald, and Paul D. Weller

## BJP

(10)

### Measuring the Long-term Impact of War-Zone Military Service Across Generations and Changing Posttraumatic Stress Disorder Definitions

Charles W. Hoge

Relationship of combat experiences to alcohol misuse among U.S. soldiers returning from the Iraq war (221)

Joshua E. Will,<sup>1\*</sup> Paul D. Bliese,<sup>2</sup> Paul V. Klim,<sup>3</sup> Jeffrey L. Thomas,<sup>4</sup> Dennis McGurk,<sup>5</sup>

(81)

Coming home may hurt: risk factors for mental health in US reservists after deployment to Iraq

Laura A. King, Jeffrey L. Thomas, Linda A. Ross, and Paul D. Weller

## ORIGINAL ARTICLE

### Prevalence of Mental Health Problems and Functional Impairment Among Active Component and National Guard Soldiers 3 and 12 Months Following Combat in Iraq

Jeffrey L. Thomas, PhD; Joshua E. Will, PhD; Linda A. Ross, PhD; Dennis McGurk, PhD; Carl A. Castro, PhD; Charles W. Hoge, MD

(85)

## JAMA

(305)

### Original Investigation

### Risk Factors Associated With Suicide in Current and Former US Military Personnel

Cynthia A. Lanzendorff, MPH; Susie M. Howell, MPH; Tracy C. Shaffer, MPH; Philip M. Hart, PhD; Michael J. Murphy, PhD; Linda A. King, PhD; and Charles W. Hoge, PhD

Journal of Traumatic Stress, Vol. 23, No. 1, February 2010, pp. 11–31 © 2010

(239)

PTSD Symptom Increases in Iraq-Deployed Soldiers: Comparison With Nondeployed Soldiers and Associations With Baseline Symptoms, Deployment Experiences, and Postdeployment Stress

Jennifer J. Vasterling,  
US Army Center for PTSD, US Army Healthcare System, and Department of Psychiatry,  
Boston University School of Medicine, Boston, MA

Susan F. Pruzek,  
US Army Center for PTSD, US Army Healthcare System, Boston, US Army Research Institute of Environmental Medicine, Natick, and Department of Environmental Health, Boston University School of Public Health, Boston, MA

Matthew J. Friedman,  
US Army Center for PTSD, White River Junction, VT, and Department of Psychiatry  
and Pharmacology, Dartmouth Medical School, Hanover, NH

Charles W. Hoge,  
Department of Psychiatry and Behavioral Sciences, Walter Reed Army Institute of Research,  
US Army Medical Research and Material Command, Silver Spring, MD

Timothy Homan,  
Department of Biostatistics, Boston University School of Public Health, Boston, MA

Linda A. King and David W. King,  
US Army Center for PTSD, US Army Healthcare System, and Department of Psychology,  
Boston University, Boston, MA

# WRAIR mTBI Clinical Research

Instrumental in delineating complex relationship between PTSD, depression, and post-concussive symptoms

- ▶ Major contribution to VA/DoD mTBI CPGs (2009 and 2015)
- ▶ Multidisciplinary collaborative strategies inform standard of care
- ▶ Revised DoD post-deployment mTBI screening tools (2011)



**Mild Traumatic Brain Injury in U.S. Soldiers Returning from Iraq**

Charles W. Hoge, M.D., Dennis B. Breyer, Ph.D., Jeffrey S. Thomas, Ph.D., Jennifer A. Guskiewicz, M.S., Michael C. Hoge, M.D., M.R.C.P., and Charles W. Luthar, Ph.D.

**Mild Traumatic Brain Injury (Concussion), Posttraumatic Stress Disorder, and Depression in U.S. Soldiers Involved in Combat Deployments: Association With Postdeployment Symptoms**

Jessica E. Wild, PhD, Richard K. Heuvel, PhD, Gary R. Wynn, MD, Lyndon A. Rymer, PhD, and Charles W. Hoge, MD

**Treatment of Generalized War-Related Health Concerns**

(21)  
Placing TBI and PTSD in Context

Charles W. Hoge, M.D., Carl A. Lederer, PhD

(11)

Indirect associations of combat exposure with post-deployment physical symptoms in U.S. soldiers: Roles of post-traumatic stress disorder, depression and insomnia

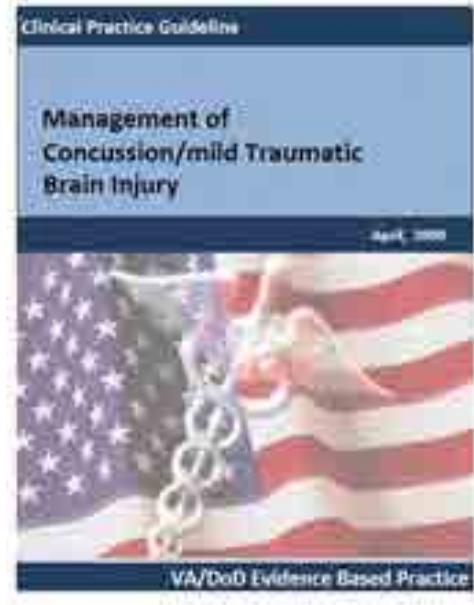
Philip J. Quartana<sup>1</sup>, Joshua E. Wild<sup>2</sup>, Thomas J. Baskin<sup>3</sup>, Charles W. Hoge<sup>4</sup>

**Journal of Affective Disorders**

(76)

Grief and physical health outcomes in U.S. soldiers returning from combat<sup>1,2</sup>

Robert L. Tilford<sup>1,2\*</sup>, Timothy A. Breslow<sup>1</sup>, Jeffrey L. Thompson<sup>1</sup>, Amy B. Apfel<sup>1,2</sup>, Brian C. Kirk<sup>1</sup>, Charles W. Hoge<sup>1</sup>

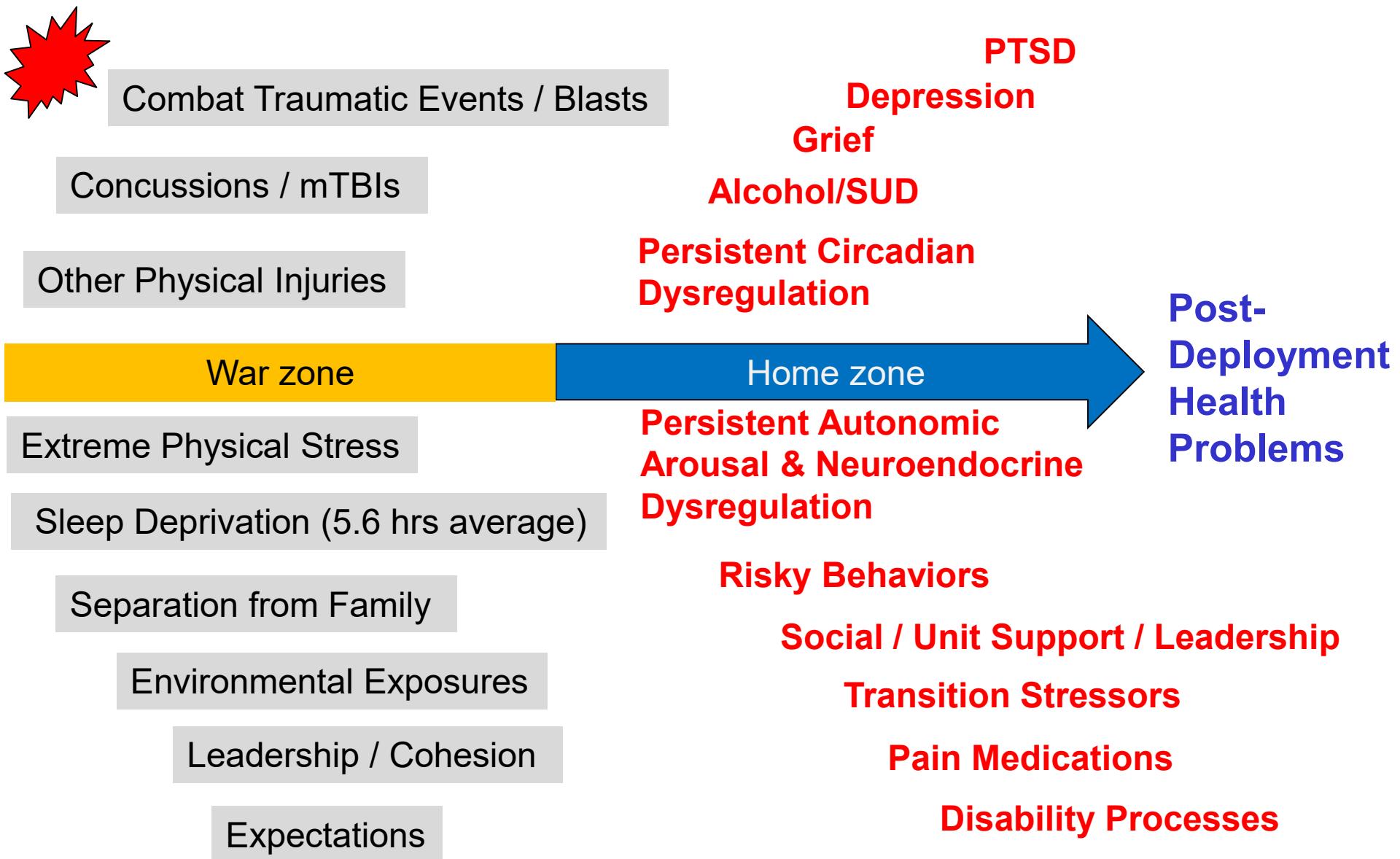


**VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF CONCUSSION-MILD TRAUMATIC BRAIN INJURY**

Department of Veterans Affairs

Department of Defense

# Contributors to Post-Deployment Health Problems



# 2008-2018—WRAIR Research Impact on Army Resilience Initiatives: Group RCTs

Journal of Traumatic Stress  
2008, Vol. 21, No. 2, 428–435

In the public domain  
DOI: 10.1007/s00707-008-0367-7

(381)

## Battlemind Debriefing and Battlemind Training as Early Interventions With Soldiers Returning From Iraq: Randomization by Platoon

Amy B. Adler

Walter Reed Army Institute of Research, Heidelberg, Germany

Paul D. Bliese

Walter Reed Army Institute of Research,  
Silver Spring, Maryland

Dennis McGurk

Walter Reed Army Institute of Research, Heidelberg, Germany

Charles W. Hoge

Walter Reed Army Institute of Research,  
Silver Spring, Maryland

Carl Andrew Castro

Medical Research and Materiel Command, Fort Detrick, Maryland

Journal of Traumatic Stress  
August 2012, Vol. 25, 356–363

CE Article



(57)

## Mental Health Training With Soldiers Four Months After Returning From Iraq: Randomization by Platoon

Carl Andrew Castro,<sup>1</sup> Amy B. Adler,<sup>2</sup> Dennis McGurk,<sup>2</sup> and Paul D. Bliese<sup>3</sup>

<sup>1</sup>Military Operational Medicine Research Program, Medical Research and Materiel Command, Frederick, Maryland, USA

<sup>2</sup>US Army Medical Research Unit-Europe, Walter Reed Army Institute of Research, Heidelberg, Germany

<sup>3</sup>Center for Military Psychiatry and Neuroscience, Walter Reed Army Institute of Research, Forest Glen, Maryland, USA

Journal of Traumatic Stress, Vol. 21, No. 2, June 2008, pp. 213–223 © 2008

(132)

## A Group Randomized Trial of Critical Incident Stress Debriefing Provided to U.S. Peacekeepers

Amy B. Adler

U.S. Army Medical Research Unit-Europe, Heidelberg, Germany, and Walter Reed Army Institute of Research, Silver Spring, Maryland

Brett T. Litz

Massachusetts General Hospital, Harvard Medical School, and Department of Psychology,  
Boston University School, MA

Carl Andrew Castro

Department of Military Psychiatry, Walter Reed Army Institute of Research, Silver Spring, MD

Michael Novak

National Center for PTSD, US Army Medical Research Institute of Psychology,  
Baltimore, Maryland, USA

Jeffrey L. Thompson, Loftus Turnbull, and Dennis McGurk

Department of Military Psychiatry, Walter Reed Army Institute of Research, Silver Spring, MD

Kathleen M. Wright and Paul D. Bliese

U.S. Army Medical Research Unit-Europe, Heidelberg, Germany, and Walter Reed Army Institute of Research, Silver Spring, MD

Journal of Traumatic Stress

In the public domain  
DOI: 10.1007/s00707-007-0367-7

(27)

## Mental Skills Training With Basic Combat Training Soldiers: A Group-Randomized Trial

Amy B. Adler and Paul D. Bliese  
Walter Reed Army Institute of Research, Silver Spring, Maryland

Michael A. Pickering and Jon Hammermester  
Eastern Washington University

Jason Williams  
Research Triangle Institute, Research Triangle Park, North Carolina

Cheyan Harada  
Army Research Institute, Crysal City, Virginia

Louis Cicali  
Apex Performance, Inc., Charlotte, North Carolina

Bernie Holliday and Carl O'Connor  
United States Military Academy

# Conclusions

- WRAIR research has played a pivotal role in addressing the mental health needs of service members and families throughout the Afghanistan and Iraq wars.
  - Mission critical operational and occupationally-relevant research
  - Timely and responsive
  - High public health impact on policies, programs, and clinical standards of care DoD-wide

# WRAIR

Walter Reed Army  
Institute of Research

# 125

YEARS  
1893-2018



Soldier Health • World Health  
UNCLASSIFIED

# At the Forefront of Research to Practice

Paul Bliese  
Professor  
Darla Moore School of Business  
University of South Carolina

14 Nov 2018



UNCLASSIFIED



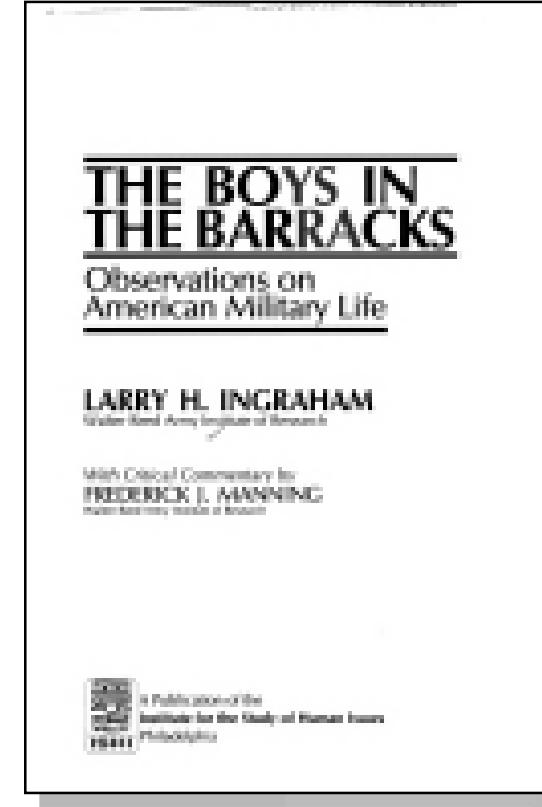
# Groups Matter



[www.history.com/news/why-were-americans-who-served-in-world-war-i-called-doughboys](http://www.history.com/news/why-were-americans-who-served-in-world-war-i-called-doughboys)

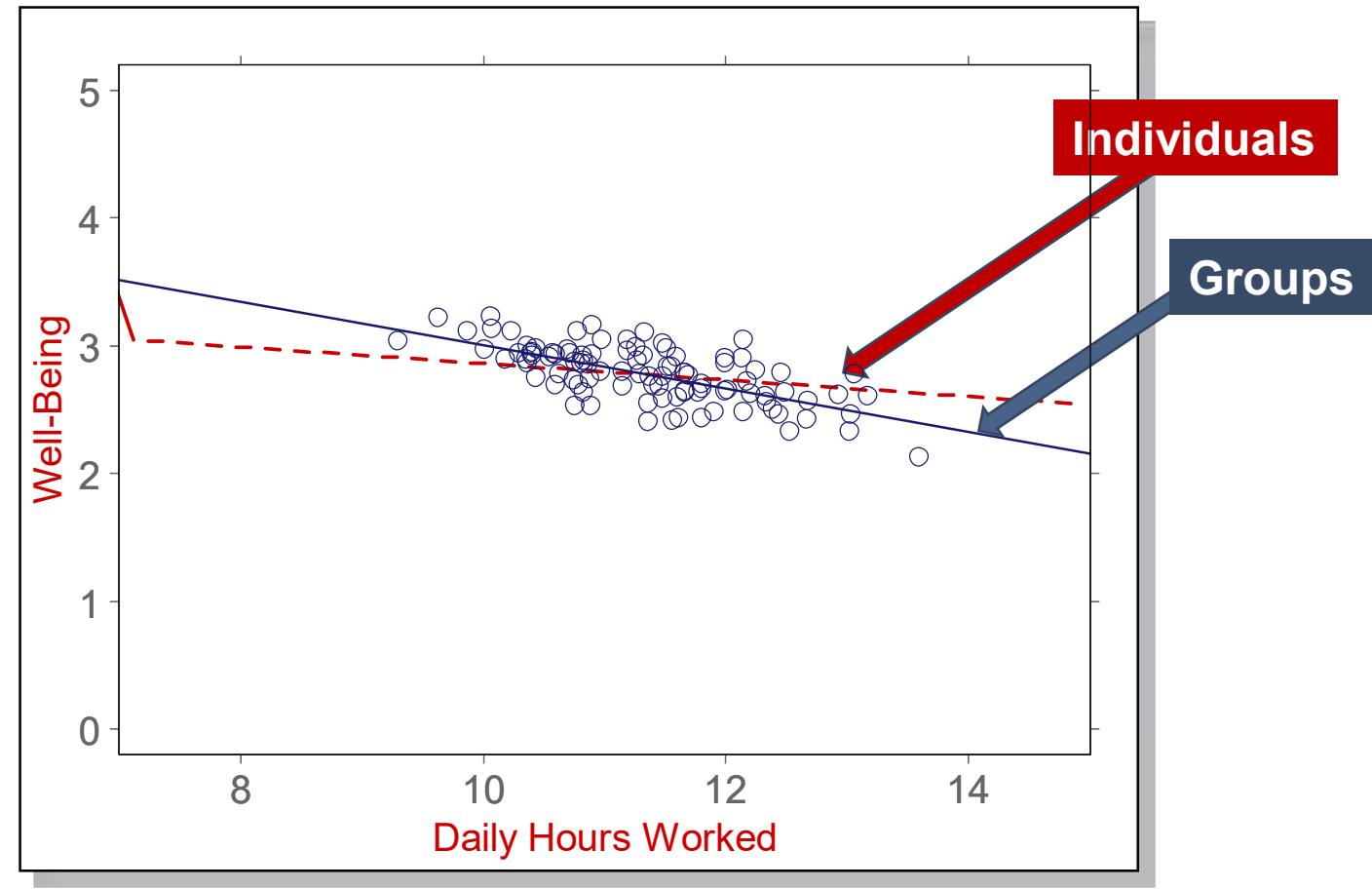


[www.vintag.es/2017/02/blow-it-out-your-barracks-bag-heres.html](http://www.vintag.es/2017/02/blow-it-out-your-barracks-bag-heres.html)



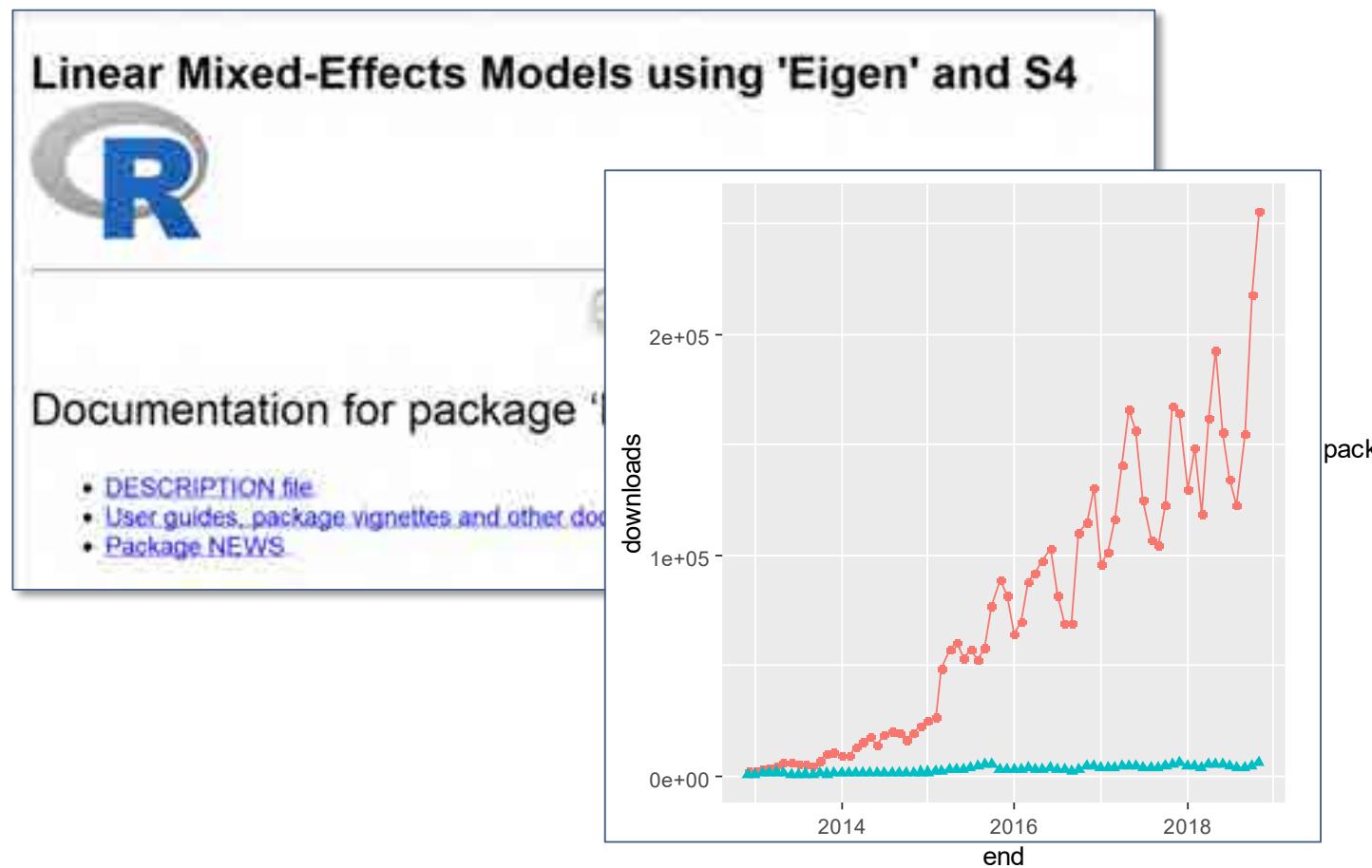
# Groups Matter

- Hard to formally test in quantitative data
- “Multilevel” theory
- Statistical models

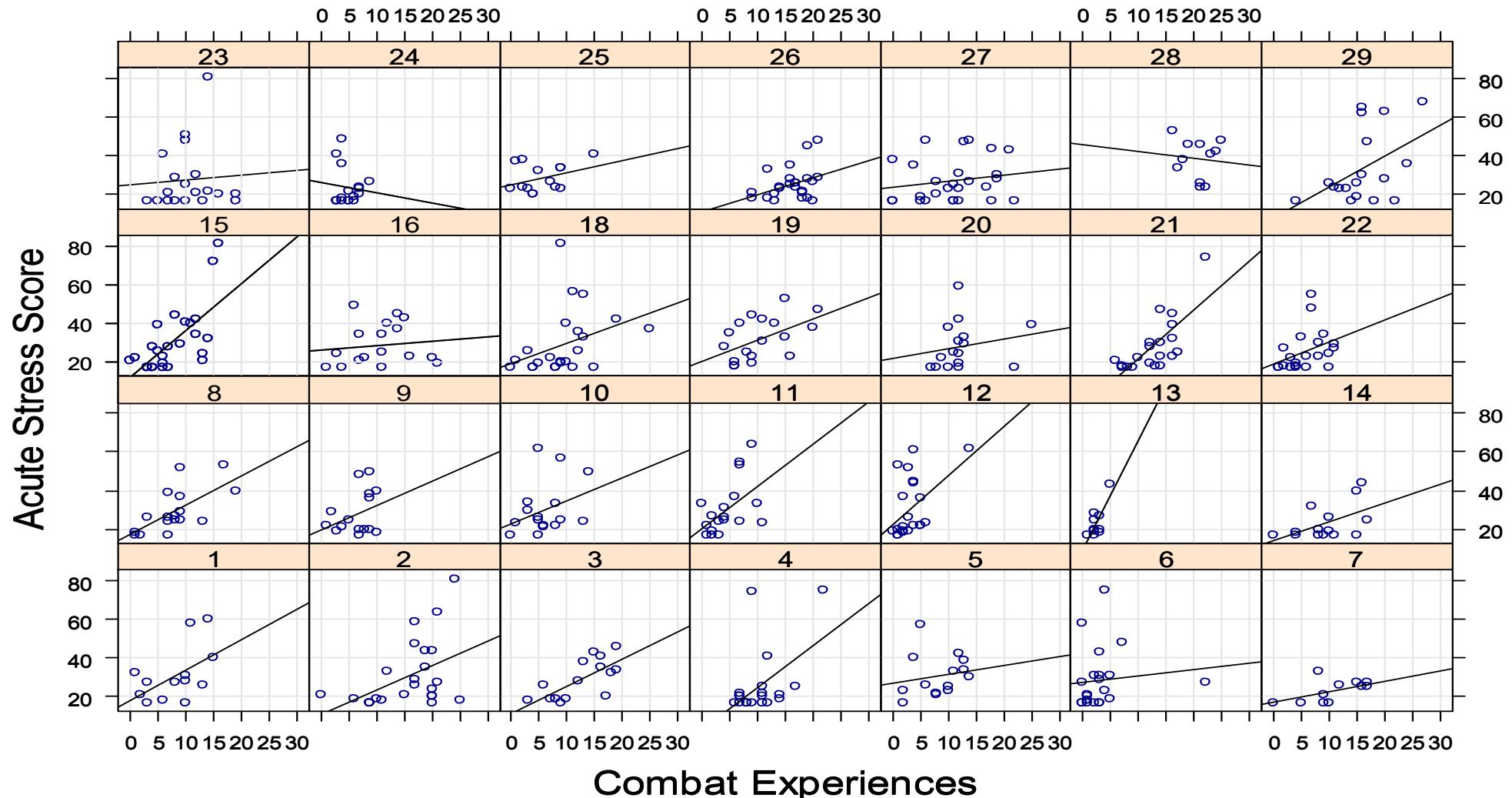


# Groups Matter

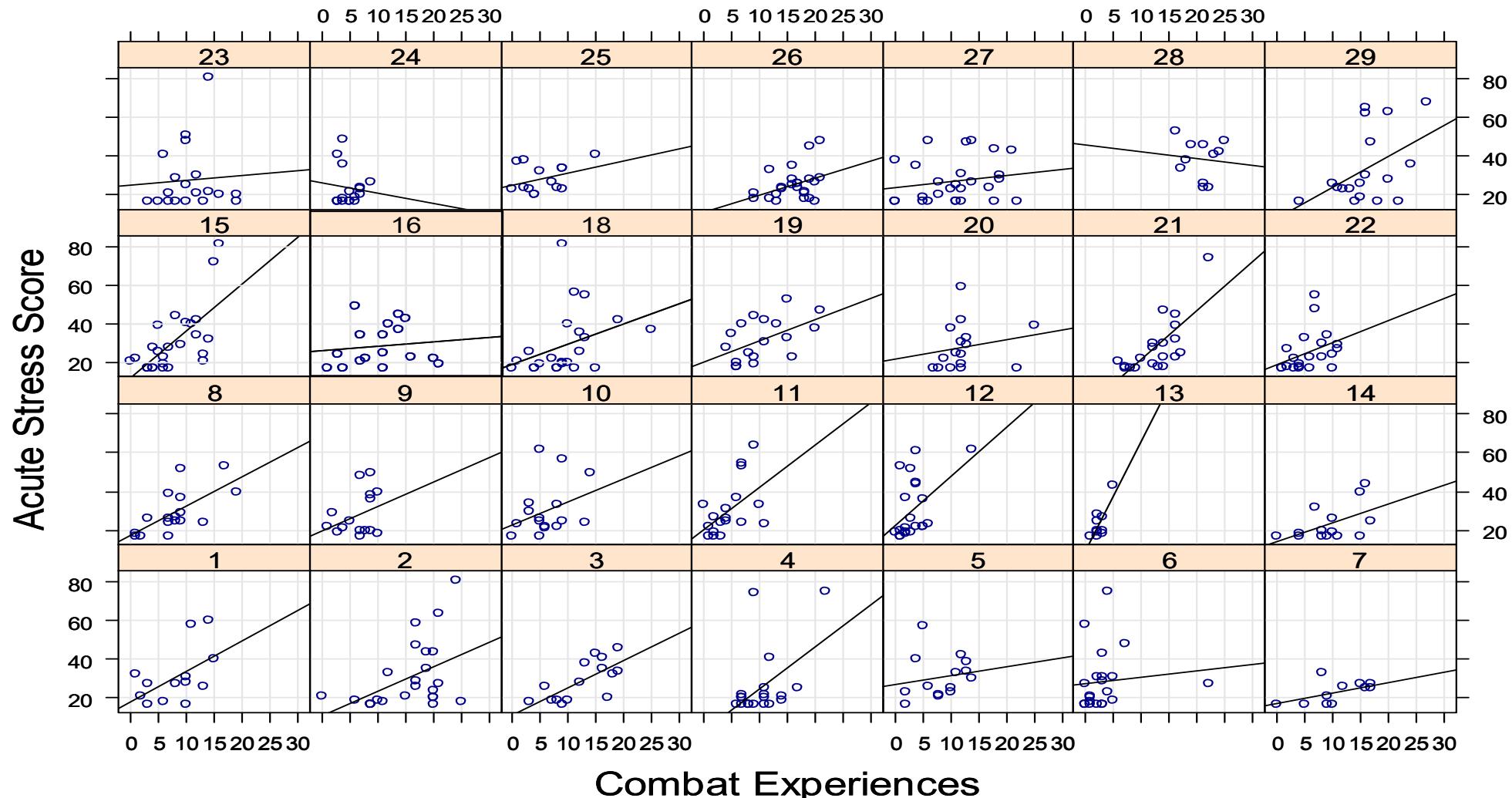
- Army-led innovations
- 250,000 downloads per month



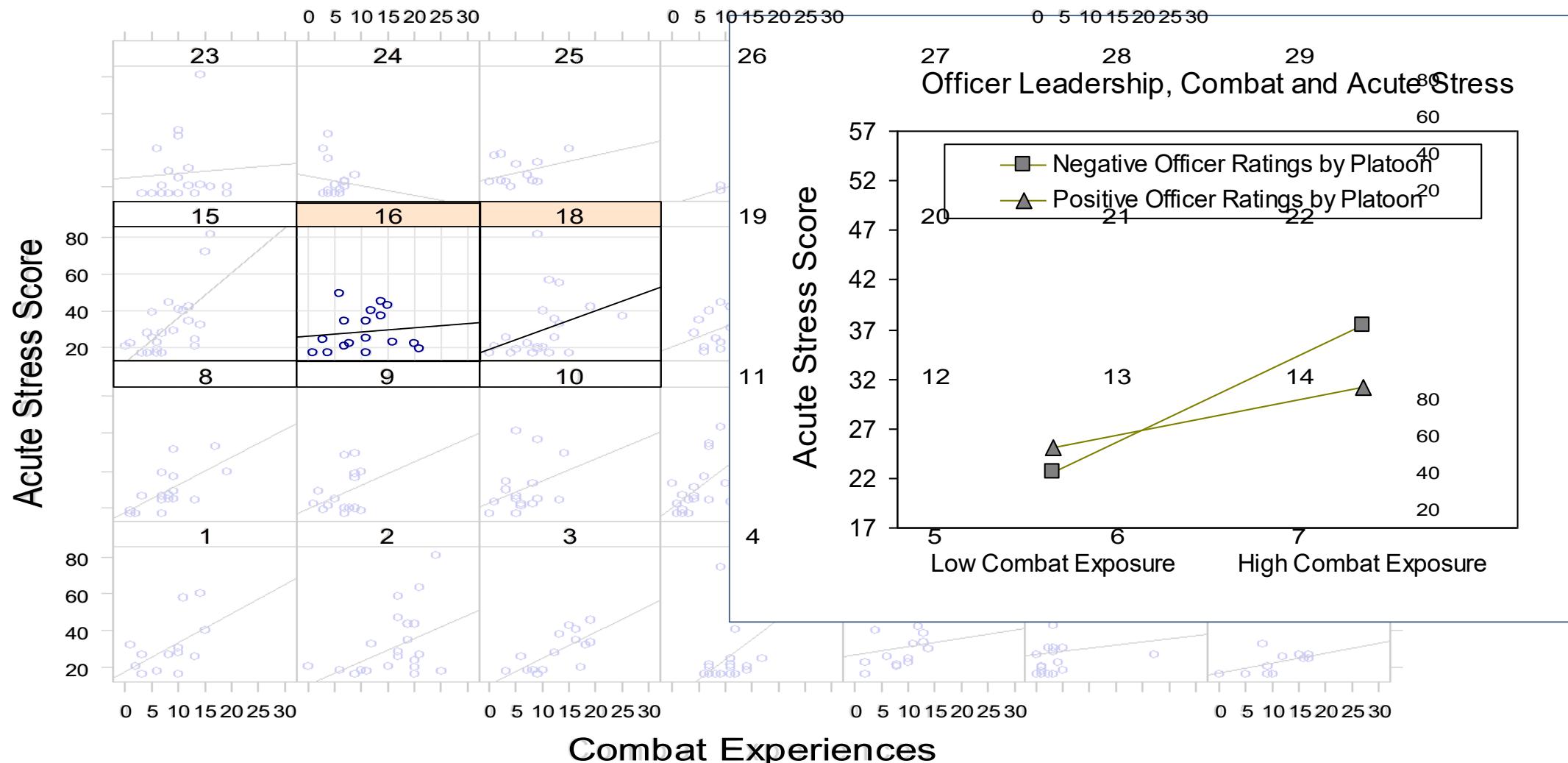
# Platoon-Level Variation



## Platoon-Level Variation



## Platoon-Level Variation



# State of the Science

- 100-year anniversary of  
**Journal of Applied Psychology**

*Journal of Applied Psychology*  
2017, Vol. 102, No. 3, 386–403  
© 2017 American Psychological Association  
0021-9010/17/\$12.00 DOI: 10.1037/ap0000109

**Stress and Well-Being at Work: A Century of Empirical Trends Reflecting Theoretical and Societal Influences**

Paul D. Bliese  
University of South Carolina

Jeffrey R. Edwards  
University of North Carolina

Sabine Sonnentag  
University of Mannheim

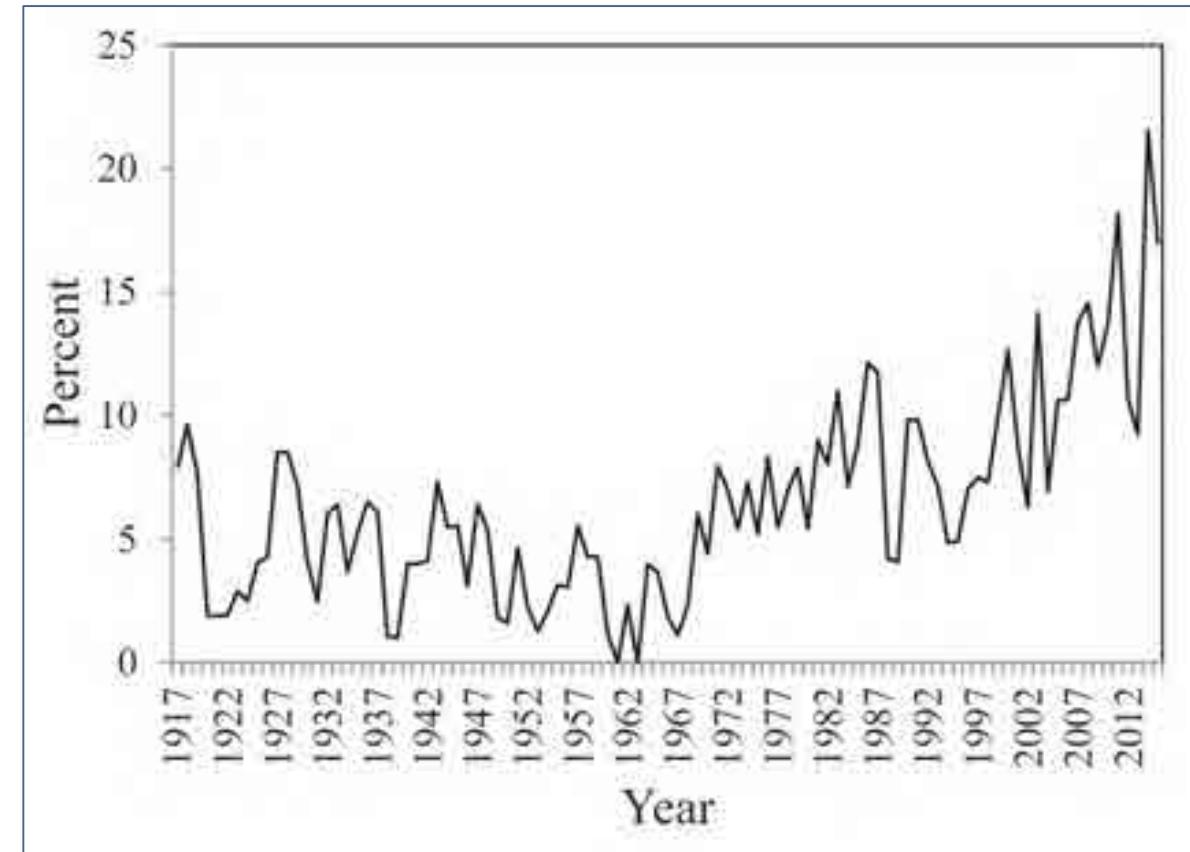
In various forms, research on stress and well-being has been a part of the *Journal of Applied Psychology* (JAP) since its inception. In this review, we examine the history of stress research in JAP by tracking word frequencies from 606 abstracts of published articles in the journal. From those abstracts, we define 3 eras: a 50-year era from 1937 to 1986, a 30-year era from 1967 to 1996, and a 20-year era from 1997 to the present. Each era is distinct in terms of the number of articles published and the general themes of the topic areas examined. We show that advances in theory are a major impetus underlying research topics and the number of publications. Our review also suggests that articles have increasingly tended to reflect broader events occurring in society such as recessions and workforce changes. We conclude by offering ideas about the future of stress and well-being research.

**Keywords:** stress; spillover; stress; health; well-being

*Supplemental materials:* <https://dx.doi.org/10.1037/ap0000109.supp>

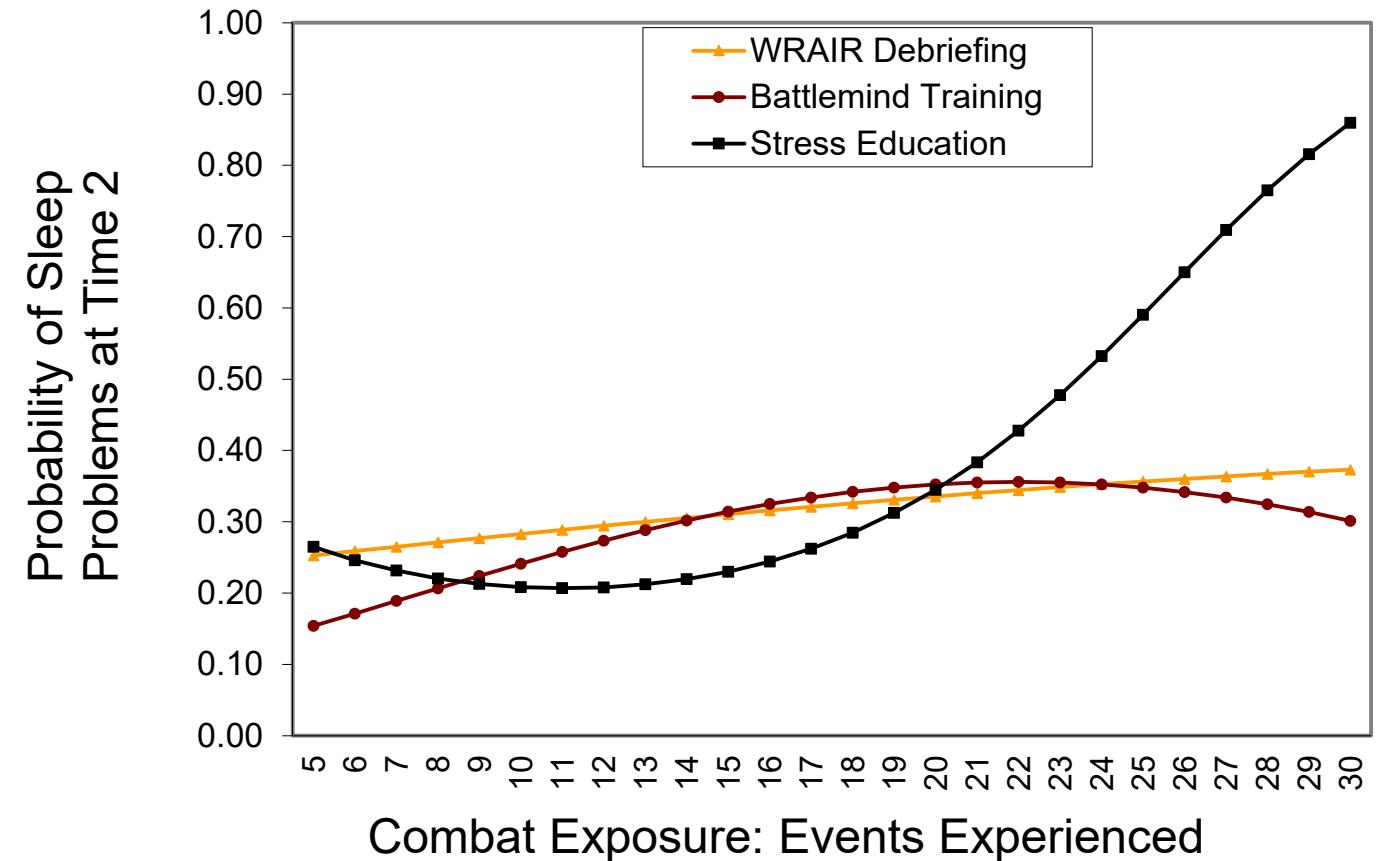
# State of the Science

- Research trends
- Only **1** randomized trial per **decade!**



# Offering Solutions

- Describe the problem
- Or...**offer solutions**



# Offering Solutions

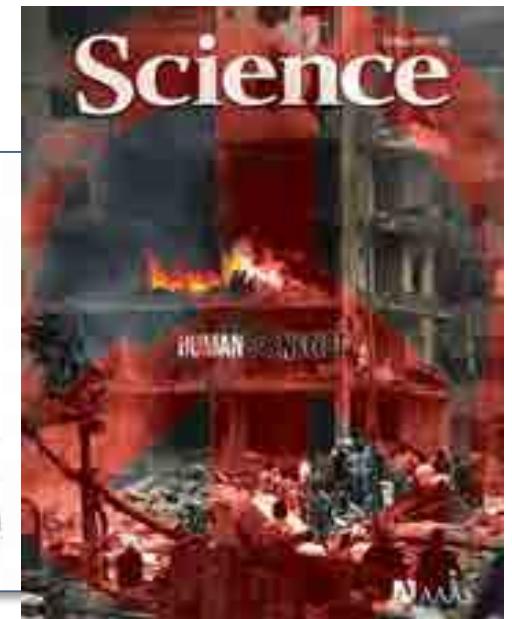
- More than a dozen randomized trials in last 15 years
- Advancing the field

PERSPECTIVE

## ARE WE WINNING THE WAR AGAINST POSTTRAUMATIC STRESS DISORDER?

Richard J. McNally

The most methodologically rigorous epidemiological study on American military personnel deployed to Iraq and Afghanistan found that 4.3% of troops developed posttraumatic stress disorder (PTSD). Among deployed combatants, 7.6% developed PTSD, whereas 3.4% of deployed noncombatants did so. The U.S. Department of Veterans Affairs has launched a program ensuring that all veterans with PTSD will receive evidence-based cognitive-behavioral therapy, and the Army has developed Battlemind postdeployment early interventions that reduce risk for the disorder.



# Real-Time Research

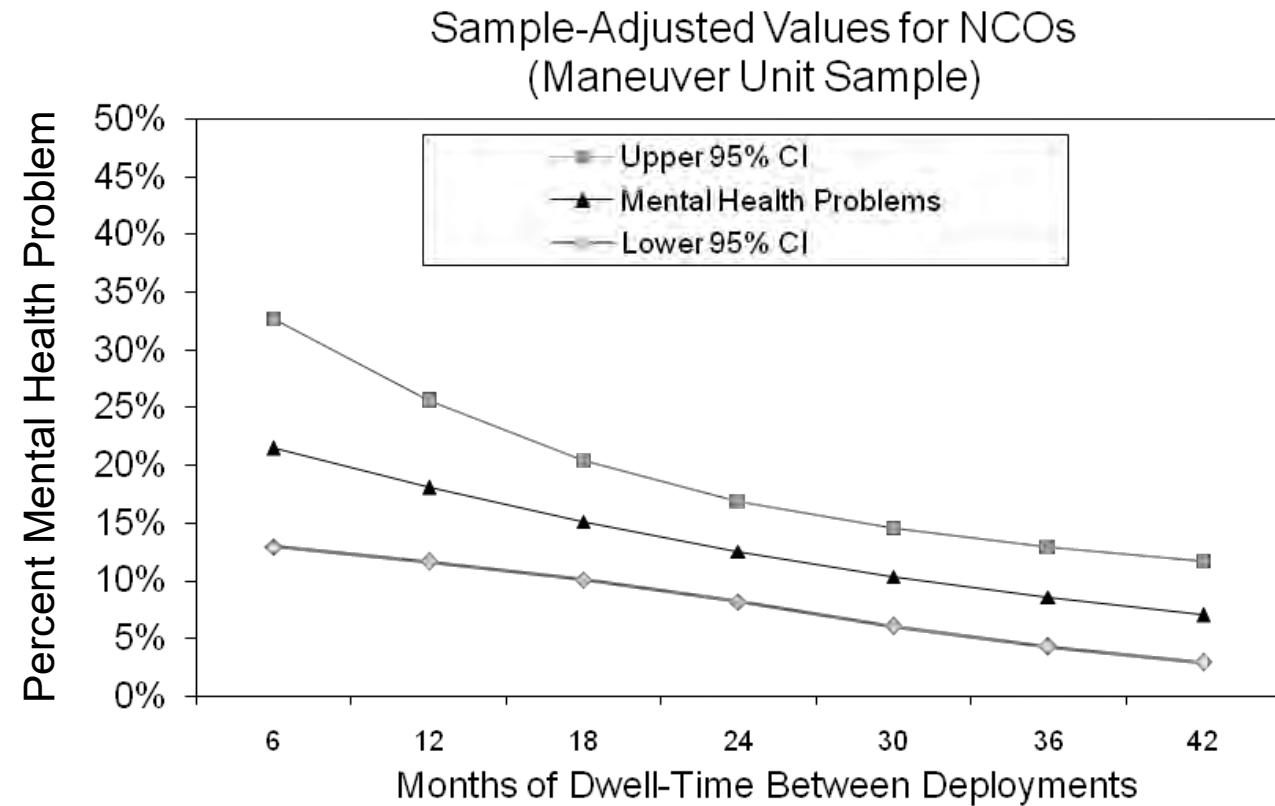
- On the ground
- Quick turn-around

1<sup>st</sup> Mental Health Advisory Team



# Real-Time Research

- Senior leader priorities
  - Multiple deployers
  - Ethics
  - Dwell time



ME SEARCH

WASHINGTON

# Army Is Worried by Rising Stress of Return Tours to Iraq

By THOM SHANKER APRIL 6, 2008

WASHINGTON — Army leaders are expressing increased alarm about the mental health of soldiers who would be sent back to the front again and

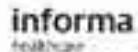


The New York Times

# Real-Time Research

- Best practices established
  - Analytics
  - Sampling

*International Review of Psychiatry*, Month 2011; 00(00): 1-8



## Mental health advisory teams: A proactive examination of mental health during combat deployments

PAUL D. BLIESE<sup>1</sup>, JEFFREY L. THOMAS<sup>1</sup>, DENNIS MCGURK<sup>1</sup>, SHARON McBRIDE<sup>2</sup>  
& CARL A. CASTRO<sup>3</sup>

<sup>1</sup> Walter Reed Army Institute of Research, Silver Spring, Maryland, <sup>2</sup> Comprehensive Soldier Fitness, Crystal City, Virginia,

<sup>3</sup> US Army Medical Research and Material Command, Frederick, Maryland

### Abstract

Mental health advisory teams (MHATs) conduct comprehensive mental health surveillance of US service members in combat environments. Since 2003, six teams have deployed to Iraq and four have deployed to Afghanistan, and results have played a key role influencing behavioural health policy. The repeated deployments of the teams have provided opportunities for processes to be refined, and this refinement has led to a scientifically rigorous and replicable approach. In this article we focus on two themes. The first theme is how changes in sampling have influenced the nature of the inferences drawn from the survey-based surveillance data. The second theme is how the ability to utilize different forms of data has served to strengthen the programme. Focusing on these two themes provides a way to discuss key findings, recommendations and limitations while also interrogating practical observations intended to help inform the design of broad-scale, in-theatre mental health surveillance efforts. We believe that future surveillance efforts should build on the lessons of the MHATs and attempt to replicate the more rigorous sampling methods; nonetheless, we also strive to convey that large surveillance efforts are valuable even if they cannot be executed with random sampling.

# **Soldier Health • World Health**

- Mainstreaming group-level research
- Promoting randomized trials in applied research
- Setting the bar for turning data into actionable information

# WRAIR

Walter Reed Army  
Institute of Research

# 125

YEARS  
1893-2018



Soldier Health • World Health  
UNCLASSIFIED